dihydrate crystal deposition disease

AUTHOR(S): Ryan, Lawrence M.; **Lynch, Michael P.**; McCarty, Daniel J.
CORPORATE SOURCE: Dep. Med., Med. Coll. Wisconsin, Milwaukee, WI, USA
SOURCE: Arthritis Rheum. (1983), 26(4), 564-6
CODEN: ARHEAW; ISSN: 0004-3591
DOCUMENT TYPE: Journal
LANGUAGE: English
CLASSIFICATION: 14-11 (Mammalian Pathological Biochemistry)
Section cross-reference(s): 13

ABSTRACT:
The total intracellular inorg. pyrophosphate (PPi) content and the fraction of PPi released (by thrombin) from the storage pool of blood platelets from normal humans, patients with sporadic Ca pyrophosphate dihydrate crystal deposition, and patients with familial disease were studied. No differences in group ranges or means were found. There appeared to be a rise in platelet PPi content with age of normal humans.

SUPPL. TERM: blood platelet inorg pyrophosphate; calcium pyrophosphate deposition disease platelet
INDEX TERM: Senescence and Senility
(inorg. pyrophosphate of blood platelet in humans in relation to)
INDEX TERM: Pseudogout
(inorg. pyrophosphate of blood platelet in, in humans)
INDEX TERM: Blood platelet
(inorg. pyrophosphate of, in primary and secondary chondrocalcinosis and health in human)
INDEX TERM: 17031-92-4
ROLE: BIOL (Biological study)
(metabolic disorders, crystal deposition disease, inorg. pyrophosphate of blood platelets in, in human)
INDEX TERM: 14000-31-9
ROLE: BIOL (Biological study)
(of blood platelets, in familial and secondary chondrocalcinosis and health in human)

L2 ANSWER 7 OF 28 BIOSIS COPYRIGHT 2001 BIOSIS
ACCESSION NUMBER: 1998:414091 BIOSIS
DOCUMENT NUMBER: PREV199800414091
TITLE: Scanning probe microscopy in biotechnology.
AUTHOR(S): **Henderson, Eric (1)**
CORPORATE SOURCE: (1) Iowa State Univ., Ames, IA USA
SOURCE: Scanning, (**April, 1998**) Vol. 20, No. 3, pp. 138.
Meeting Info.: Scanning 98: Meeting of the Foundation for Advances in Medicine and Science Baltimore, Maryland, USA May 10-12, 1998 Foundation for Advances in Medicine and Science
. ISSN: 0161-0457.
DOCUMENT TYPE: Conference
LANGUAGE: English
CONCEPT CODE: Microscopy Techniques - General and Special Techniques *01052
Genetics and Cytogenetics - General *03502
Biochemical Studies - Nucleic Acids, Purines and Pyrimidines *10062
Biophysics - General Biophysical Techniques *10504
Biophysics - Bioengineering *10511
General Biology - Symposia, Transactions and Proceedings of Conferences, Congresses, Review Annuals *00520
INDEX TERMS: Major Concepts
Bioprocess Engineering; Methods and Techniques
INDEX TERMS: Methods & Equipment
atomic force microscopy: microscopy method
INDEX TERMS: Miscellaneous Descriptors
biotechnology; Meeting Abstract

L2 ANSWER 17 OF 28 BIOSIS COPYRIGHT 2001 BIOSIS
ACCESSION NUMBER: 1997:119181 BIOSIS
DOCUMENT NUMBER: PREV199799425684
TITLE: Chicken erythrocyte nucleosomes have a defined orientation along the linker DNA: A scanning force microscopy study.
AUTHOR(S): Fritzche, Wolfgang (1); **Henderson, Eric**
CORPORATE SOURCE: (1) Inst. Phys. High Technol., Dep. Cryoelectronics Microsystems, P.O. Box 100 239, D-07702 Jena Germany
SOURCE: Scanning, (1997) Vol. 19, No. 1, pp. 42-47.
ISSN: 0161-0457.
DOCUMENT TYPE: Article
LANGUAGE: English
ABSTRACT:
The orientation of nucleosomes was investigated using scanning force microscopy (SFM) of hypotonically spread chicken chromatin. A virtual cross section parallel to the substrate at half maximum height of the nucleosomal structure revealed an elliptical shape. The orientation of the major axis of this ellipse was investigated in reference to the direction of the axis of the nucleosomal chain. An alignment of the nucleosomes along the nucleosomal chain was observed, with more than 50% of the nucleosomes aligned with the long axis of the chain within ltoreq 30 degree deviation. The alignment distribution peaked at 10-20 degree . The application of SFM-based image processing for the structural investigation of a protein-DNA complex demonstrates the potential for this approach in structural molecular biology.
CONCEPT CODE: Microscopy Techniques - General and Special Techniques *01052
Cytology and Cytochemistry - Animal *02506
Biochemical Studies - Nucleic Acids, Purines and Pyrimidines *10062
Biochemical Studies - Proteins, Peptides and Amino Acids *10064
Blood, Blood-Forming Organs and Body Fluids - Blood Cell Studies *15004
BIOSYSTEMATIC CODE: Galliformes *85536
INDEX TERMS: Major Concepts
Biochemistry and Molecular Biophysics; Blood and Lymphatics (Transport and Circulation); Cell Biology; Methods and Techniques
INDEX TERMS: Miscellaneous Descriptors
BLOOD AND LYMPHATICS; CELL BIOLOGY; CHROMATIN; DNA; DNA-PROTEIN COMPLEX; ERYTHROCYTE; IMAGE PROCESSING; METHODOLOGY; MICROSCOPY METHOD; NUCLEOSOMES; SCANNING FORCE MICROSCOPY
ORGANISM: Super Taxa
Galliformes: Aves, Vertebrata, Chordata, Animalia
ORGANISM: Organism Name
chicken (Galliformes)
ORGANISM: Organism Superterms
animals; birds; chordates; nonhuman vertebrates; vertebrates

L2 ANSWER 22 OF 28 BIOSIS COPYRIGHT 2001 BIOSIS
ACCESSION NUMBER: 1995:315199 BIOSIS
DOCUMENT NUMBER: PREV199598329499
TITLE: Imaging and manipulating chromosomes with the atomic force microscope.
AUTHOR(S): Jondle, Daniel M.; Ambrosio, Linda; Vesenka, James; **Henderson, Eric (1)**
CORPORATE SOURCE: (1) Dep. Zool. Genet., Iowa State Univ., Ames, IA 50011 USA
SOURCE: Chromosome Research, (1995) Vol. 3, No. 4, pp. 239-244. ISSN: 0967-3849.
DOCUMENT TYPE: Article
LANGUAGE: English
ABSTRACT:
Polytene chromosomes from the salivary gland cells of Drosophila melanogaster were examined by atomic force microscopy. The atomic force microscope (AFM) was capable of resolving chromosomal features down to the limits of the tip sharpness, about 500 ANG for pyramidal-shaped tips. Resolution was increased to 300 ANG by using electron beam deposited (EBD) tips with high aspect ratios. This significantly exceeds the resolution obtainable with conventional optical microscopes, but at the cost of compromising the structural integrity of the sample. A reasonable compromise was achieved by using oxide-sharpened tips. In this case high resolution was obtained without sample degradation, but when desired these tips were also capable of sample disintegration with increased scanning force and rate. Thus, oxide-sharpened tips were used to precisely dissect defined chromosomal regions to illustrate their potential use in genetic mapping efforts. This study illustrates the utility of the AFM in the characterization and manipulation of chromosomes and chromosomal DNA.
CONCEPT CODE: Microscopy Techniques - General and Special Techniques 01052
Genetics and Cytogenetics - Animal *03506
Biochemical Studies - Nucleic Acids, Purines and Pyrimidines 10062
Anatomy and Histology, General and Comparative - Microscopic and Ultramicroscopic Anatomy *11108
Invertebrata, Comparative and Experimental Morphology, Physiology and Pathology - Insecta - Physiology *64076
BIOSYSTEMATIC CODE: Diptera *75314
INDEX TERMS: Major Concepts
Genetics; Morphology; Physiology
INDEX TERMS: Miscellaneous Descriptors
POLYTENE CHROMOSOME; ULTRASTRUCTURE
ORGANISM: Super Taxa
Diptera: Insecta, Arthropoda, Invertebrata, Animalia
ORGANISM: Organism Name
Drosophila melanogaster (Diptera)
ORGANISM: Organism Superterms
animals; arthropods; insects; invertebrates

L3 ANSWER 1 OF 16 BIOSIS COPYRIGHT 2001 BIOSIS
ACCESSION NUMBER: 2000:544893 BIOSIS
DOCUMENT NUMBER: PREV200000544893
TITLE: The effect of super-oxidized water on Escherichia coli.
AUTHOR(S): Zinkevich, V. (1); Beech, I. B.; Tapper, R.; Bogdarina, I.
CORPORATE SOURCE: (1) School of Pharmacy and Biomedical Sciences, University of Portsmouth, White Swan Road, St. Michael's Building, Portsmouth, PO1 2DT UK
SOURCE: Journal of Hospital Infection, (October, 2000) Vol. 46, No. 2, pp. 153-156. print.
ISSN: 0195-6701.
DOCUMENT TYPE: Article
LANGUAGE: English
SUMMARY LANGUAGE: English
ABSTRACT:
The mechanism of action of Sterilox, a non-toxic liquid biocide produced by electrolysis of a dilute saline solution, upon planktonic cells of Escherichia coli JM109 was investigated using protein and **nucleic** acid analysis. The results revealed total destruction of chromosomal and plasmid **DNA**, RNA and proteins of E. coli within 5 min of exposure. Our earlier investigation conducted using **atomic force** ***microscopy*** imaging revealed swelling and rupture of E. coli cells with release of cytoplasm. We propose that the biocidal properties of Sterilox are due to its effect upon constituents of the bacterial cell including proteins and **nucleic** acids.
CONCEPT CODE: Physiology and Biochemistry of Bacteria *31000
Biochemical Studies - Nucleic Acids, Purines and Pyrimidines *10062
Biochemical Studies - Proteins, Peptides and Amino Acids *10064
Public Health: Environmental Health - Sewage Disposal and Sanitary Measures *37014
Pest Control, General; Pesticides; Herbicides *54600
BIOSYSTEMATIC CODE: Enterobacteriaceae 06702
INDEX TERMS: Major Concepts
Sanitation
INDEX TERMS: Chemicals & Biochemicals
Sterilox: biocide; plasmid **DNA**; plasmid RNA; proteins; super-oxidized water
INDEX TERMS: Methods & Equipment
electrolysis: synthetic method; **nucleic** acid analysis: analytical method; protein analysis: analytical method
ORGANISM: Super Taxa
Enterobacteriaceae: Facultatively Anaerobic Gram-Negative Rods, Eubacteria, Bacteria, Microorganisms; Hominidae: Primates, Mammalia, Vertebrata, Chordata, Animalia
ORGANISM: Organism Name
Escherichia coli (Enterobacteriaceae): pathogen, strain-JM109; human (Hominidae): patient
ORGANISM: Organism Superterms
Animals; Bacteria; Chordates; Eubacteria; Humans; Mammals; Microorganisms; Primates; Vertebrates

L3 ANSWER 2 OF 16 BIOSIS COPYRIGHT 2001 BIOSIS
ACCESSION NUMBER: 2000:497584 BIOSIS
DOCUMENT NUMBER: PREV200000497705
TITLE: Near field microscopies: From isolated molecules to living cells.
AUTHOR(S): Delain, E. (1); Michel, D. (1); Le Grimellec, Ch.
CORPORATE SOURCE: (1) Laboratoire de Microscopie Moleculaire et Cellulaire/CNRS UMR 8532, Institut Gustave Roussy, Rue Camille Desmoulins, Villejuif France
SOURCE: Morphologie, (Juin, 2000) Vol. 84, No. 265, pp. 25-30.

print.
ISSN: 1286-0115.
DOCUMENT TYPE: Article
LANGUAGE: French
SUMMARY LANGUAGE: English; French
ABSTRACT:
Near field (or scanning probe) **microscopy** is a recent technology which, owing to the huge amount of publications, is becoming a reference method in molecular and cellular imaging. These microscopies consist in the scanning of the sample, line by line, with a very tiny tip and thus providing informations on its surface down to the nanometer scale. These methods gather scanning tunelling **microscopy** (STM), which measures a current between the tip and the specimen support, **atomic force** ***microscopy*** (AFM), which measures the repulsive and attractive forces of the tip in contact or very close to the specimen, and scanning near field optical microscopies (SNOM), for which a glass tip allows to catch light signals. **Atomic force microscopy**, which allows the observation of specimens in air or physiological conditions environments, is presently dominant in biology, in complementarity with the classical optical and electron microscopies, which by the way, have also shown considerable improvements during the last years. The complementarity of these microscopies is due to their very different basic principles, which provide them various possibilities and limits. The biological applications of STM is limited by the need of conducting samples, but the different models of SNOM, often still is development, allow to consider very interesting applications, particularly for detecting very faint and tiny fluorescence signals. Different examples will be given concerning the visualization by AFM of isolated **DNA** molecules, naked or associated with proteins, the observation of intact or decondensed chromosomes, as well as living cells. One of the originality of AFM is its capacity to observed objects in a wide range of enlargements, with fields from a few hundred of nanometers to several micrometers.
CONCEPT CODE: Cytology and Cytochemistry - General *02502
Biochemical Studies - General *10060
Biochemical Studies - Nucleic Acids, Purines and Pyrimidines *10062
Biochemical Studies - Proteins, Peptides and Amino Acids *10064
INDEX TERMS: Major Concepts
Biochemistry and Molecular Biophysics; Cell Biology; Methods and Techniques
INDEX TERMS: Parts, Structures, & Systems of Organisms
cells: near field microscopic study
INDEX TERMS: Chemicals & Biochemicals
double stranded **DNA**: microscopic study; **nucleic** acids: microscopic study; proteins: microscopic study
INDEX TERMS: Methods & Equipment
scanning near field optical **microscopy**: analytical method; scanning probe **microscopy** [near field **microscopy**]: analytical method
ORGANISM: Super Taxa
Organisms
ORGANISM: Organism Name
organism (Organisms)

L3 ANSWER 3 OF 16 BIOSIS COPYRIGHT 2001 BIOSIS
ACCESSION NUMBER: 2000:309262 BIOSIS
DOCUMENT NUMBER: PREV200000309262
TITLE: A dimer as a building block in assembling RNA: A hexamer that gears bacterial virus phi29 **DNA** -translocating machinery.
AUTHOR(S): Chen, Chaoping; Sheng, Sitong; Shao, Zhifeng; Guo, Peixuan
SOURCE: Journal of Biological Chemistry, (June 9, 2000), Vol. 275, No. 23, pp. 17510-17516. print.

ISSN: 0021-9258.
DOCUMENT TYPE: Article
LANGUAGE: English
SUMMARY LANGUAGE: English
ABSTRACT:
Six RNA (pRNA) molecules form a hexamer, via hand-in-hand interaction, to gear bacterial virus phi29 **DNA** translocation machinery. Here we report the pathway and the conditions for the hexamer formation. Stable pRNA dimers and trimers were assembled in solution, isolated from native gels, and separated by sedimentation, providing a model system for the study of RNA dimers and trimers in a protein-free environment. Cryoatomic **force microscopy** revealed that monomers displayed a check-mark shaped outline, dimers exhibited an elongated shape, and trimers formed a triangle. Dimerization of pRNA was promoted by a variety of cations including spermidine, whereas procapsid binding and **DNA** packaging required specific divalent cations, including Mg2+, Ca2+, and Mn2+. Both the tandem and fused pRNA dimers with complementary loops designed to form even-numbered rings were active in ***DNA*** packaging, whereas those without complementary loops were inactive. We conclude that dimers are the building blocks of the hexamer, and the pathway of building a hexamer is: dimer fwdarw tetramer fwdarw hexamer. The Hill coefficient of 2.5 suggests that there are three binding sites with cooperative binding on the surface of the procapsid. The two interacting loops played a key role in recruiting the incoming dimer, whereas the procapsid served as the foundation for hexamer assembly.
CONCEPT CODE: Biochemical Studies - Nucleic Acids, Purines and Pyrimidines *10062
Methods, Materials and Apparatus, General - Laboratory Methods *01004
Virology - Animal Host Viruses *33506
Biochemical Studies - Minerals *10069
INDEX TERMS: Major Concepts
Biochemistry and Molecular Biophysics; Methods and Techniques
INDEX TERMS: Chemicals & Biochemicals
DNA-translocating machinery; RNA: assay, isolation, separation, synthesis; calcium (II); magnesium (II); manganese (II)
INDEX TERMS: Methods & Equipment
PAGE [polyacrylamide gel electrophoresis]: gel electrophoresis, isolation method; RNA binding assay: analytical method, binding assays; RNA synthesis: **nucleic** acid synthesis, synthetic method; cryo-**atomic force microscopy** [cryo-AFM]: **microscopy** method, **microscopy** : CB; dimer binding competition assay: Analysis/Characterization Techniques: CB, analytical method; sucrose gradient sedimentation: Extraction, Isolation, Purification and Separation Techniques, separation method; virion assembly assay: Analysis/Characterization Techniques: CB, analytical method
ORGANISM: Super Taxa
Podoviridae: Bacterial Viruses, Viruses, Microorganisms
ORGANISM: Organism Name
phi29 (Podoviridae)
ORGANISM: Organism Superterms
Bacterial Viruses; Microorganisms; Viruses
REGISTRY NUMBER: 14127-61-8 (CALCIUM (II))
22537-22-0 (MAGNESIUM (II))
16397-91-4 (MANGANESE (II))

L3 ANSWER 4 OF 16 BIOSIS COPYRIGHT 2001 BIOSIS
ACCESSION NUMBER: 2000:246496 BIOSIS
DOCUMENT NUMBER: PREV200000246496
TITLE: PNA-dependent gene chemistry: Stable coupling of peptide

and oligonucleotides to plasmid **DNA**.
AUTHOR(S): Zelphati, O.; Liang, X.; Nguyen, C.; Barlow, S.; Sheng, S.; Shao, Z.; Felgner, P. L. (1)
CORPORATE SOURCE: (1) Gene Therapy Systems, 10190 Telesis Court, San Diego, CA, 92121 USA
SOURCE: Biotechniques, (Feb., 2000) Vol. 28, No. 2, pp. 304-316. ISSN: 0736-6205.
DOCUMENT TYPE: Article
LANGUAGE: English
SUMMARY LANGUAGE: English
ABSTRACT:
Two approaches are described for stably conjugating peptides, proteins and oligonucleotides onto plasmid **DNA**. Both methods use a peptide ***nucleic*** acid (PNA) clamp, which binds irreversibly and specifically to a binding site cloned into the plasmid. The first approach uses a biotin-conjugated PNA clamp that can be used to introduce functional biotin groups onto the plasmid to which streptavidin can bind. **Atomic** ***force*** **microscopy** images of linearized plasmid show streptavidin localized at the predicted PNA binding site on the **DNA** strand. Peptides and oligonucleotides containing free thiol groups were conjugated to maleimide streptavidin, and these streptavidin conjugates were bound to the biotin-PNA-labeled plasmid. In this way, peptides and oligonucleotides could be brought into stable association with the plasmid. A second approach used a maleimide-conjugated PNA clamp. Methods are described for conjugating thiolated peptides and oligonucleotides directly to the maleimide-PNA-**DNA** hybrid. This straightforward technology offers an easy approach to introduce functional groups onto plasmid **DNA** without disturbing its transcriptional activity.
CONCEPT CODE: Biochemical Methods - Nucleic Acids, Purines and Pyrimidines *10052
Biochemical Studies - Proteins, Peptides and Amino Acids *10064
Biophysics - General Biophysical Techniques *10504
Genetics of Bacteria and Viruses *31500
INDEX TERMS: Major Concepts
Molecular Genetics (Biochemistry and Molecular Biophysics); Methods and Techniques
INDEX TERMS: Chemicals & Biochemicals
oligonucleotides; peptide **nucleic** acid; peptides; plasmid **DNA**
INDEX TERMS: Methods & Equipment
ATTO-TAG labeling kit: Molecular Probes, equipment; agarose gel electrophoresis: analytical method, gel electrophoresis; **atomic force** **microscopy**: **microscopy** method, **microscopy**: CB, **microscopy**: CT; transfection: gene expression/vector techniques, genetic method; transmission electron **microscopy**: electron **microscopy**: CB, electron **microscopy**: CT, **microscopy** method
INDEX TERMS: Miscellaneous Descriptors
PNA-dependent gene chemistry

L3 ANSWER 5 OF 16 BIOSIS COPYRIGHT 2001 BIOSIS
ACCESSION NUMBER: 2000:61886 BIOSIS
DOCUMENT NUMBER: PREV200000061886
TITLE: Polymerase activities and RNA structures in the **atomic force** microscope.
AUTHOR(S): Hansma, Helen G. (1); Golan, Roxana; Hsieh, Wan; Daubendiek, Sarah L.; Kool, Eric T.
CORPORATE SOURCE: (1) Department of Physics, University of California, Santa Barbara, Santa Barbara, CA USA
SOURCE: Journal of Structural Biology, (Oct., 1999) Vol. 127, No. 3, pp. 240-247.

ISSN: 1047-8477.
DOCUMENT TYPE: Article
LANGUAGE: English
SUMMARY LANGUAGE: English
ABSTRACT:
The structures of the reaction products are the basis for novel polymerase assays using the **atomic force** microscope (AFM). Polymerases are the enzymes involved in transcription and replication of **DNA**. Rapid semiquantitative estimates of the activity of **DNA** polymerases such as Sequenase, Taq polymerase, and AMV reverse transcriptase and RNA polymerases (RNAP) such as Escherichia coli RNAP were obtained from AFM images of the **nucleic** acids after polymerase reactions. **DNA** polymerases were assayed via replication of the single-stranded PHIX-174 virion. RNAP was assayed via transcription, using a rolling circle **DNA** template that produces long strands of RNA. In some cases, AFM was better than agarose gel electrophoresis for assaying **DNA** polymerase activity, since aggregation prevented the **DNA** from entering the agarose ge.. Extended molecules of single-stranded RNA synthesized with the rolling circle ***DNA*** template showed varied conformations and degrees of stretching. Some structural differences were observed between two RNAs-a ribozyme concatamer and an RNA with 90% purines.
CONCEPT CODE: Genetics and Cytogenetics - General *03502
Microscopy Techniques - Electron Microscopy *01058
Biochemical Methods - Nucleic Acids, Purines and Pyrimidines *10052
Biochemical Studies - Nucleic Acids, Purines and Pyrimidines *10062
Replication, Transcription, Translation *10...
Biophysics - Molecular Properties and Macromolecules *10506
Enzymes - Methods *10804
Enzymes - Chemical and Physical *10806
Physiology and Biochemistry of Bacteria *31000
Genetics of Bacteria and Viruses *31500
Virology - General; Methods *33502
BIOSYSTEMATIC CODE: Microviridae 02706
Enterobacteriaceae 06702
INDEX TERMS: Major Concepts
Enzymology (Biochemistry and Molecular Biophysics); Molecular Genetics (Biochemistry and Molecular Biophysics)
INDEX TERMS: Chemicals & Biochemicals
AMV reverse transcriptase; **DNA**: rolling circle template; **DNA** polymerase; RNA: structure; RNA polymerase; Taq polymerase
INDEX TERMS: Methods & Equipment
atomic force microscope: laboratory equipment; **atomic force microscopy**: analytical method, **microscopy**: CB, molecular imaging method
ORGANISM: Super Taxa
Enterobacteriaceae: Facultatively Anaerobic Gram-Negative Rods, Eubacteria, Bacteria, Microorganisms; Microviridae: Bacterial Viruses, Viruses, Microorganisms
ORGANISM: Organism Name
Escherichia coli (Enterobacteriaceae ; bacteria; ...
phi-X-174 (Microviridae)
ORGANISM: Organism Superterms
Bacteria; Bacterial Viruses; Eubacteria; Microorganisms; Viruses
REGISTRY NUMBER: 9012-90-2 (**DNA** POLYMERASE)
9014-24-8 (RNA POLYMERASE)

L3 ANSWER 6 OF 16 BIOSIS COPYRIGHT 2001 BIOSIS
ACCESSION NUMBER: 2000:2359 BIOSIS

DOCUMENT NUMBER: PREV200000002359
TITLE: **DNA** toroids: Stages in condensation.
AUTHOR(S): Golan, Roxana; Pietrasanta, Lia I.; Hsieh, Wan; Hansma, Helen G. (1)
CORPORATE SOURCE: (1) Department of Physics, UCSB, Santa Barbara, CA, 93106 USA
SOURCE: Biochemistry, (Oct. 19, 1999) Vol. 38, No. 42, pp. 14069-14076.
ISSN: 0006-2960.
DOCUMENT TYPE: Article
LANGUAGE: English
SUMMARY LANGUAGE: English
ABSTRACT:
The effects of polylysine (PLL) and PLL-asialoorosomucoid (AsOR) on **DNA** condensation have been analyzed by AFM. Different types of condensed ***DNA*** structures were observed, which show a sequence of conformational changes as circular plasmid **DNA** molecules condense progressively. The structures range from circular molecules with the length of the plasmid ***DNA*** to small toroids and short rods with apprx1/6 to 1/8 the contour length of the uncondensed circular **DNA**. Single plasmid molecules of 6800 base pairs (bp) condense into single toroids of apprx110 nm diameter, measured center-to-center. The results are consistent with a model for ***DNA*** condensation in which circular **DNA** molecules fold several times into progressively shorter rods. Structures intermediate between toroids and rods suggest that at least some toroids may form by the opening up of rods as proposed by Dunlap et al. ((1997) **Nucleic** Acids Res. 25, 3095). Toroids and rods formed at lysine:nucleotide ratios of 5:1 and 6:1. This high lys ine: nucleotide ratio is discussed in relation to entropic considerations and the overcharging of macroions. PLL-AsOR is much more effective than PLL alone for condensing **DNA**, because several PLL molecules are attached to a single AsOR molecule, resulting in an increased cation density.
CONCEPT CODE: Genetics and Cytogenetics - General *03502
Microscopy Techniques - General and Special Techniques *01052
Biochemical Methods - General *10050
Biochemical Studies - General *10060
Biophysics - General Biophysical Studies *10502
INDEX TERMS: Major Concepts
Molecular Genetics (Biochemistry and Molecular Biophysics ; Methods and Techniques
INDEX TERMS: Chemicals & Biochemicals
DNA toroids: analysis, condensation stages; polylysine: **DNA** condenser; polylysine-asialoorosomucoid: **DNA** condenser
INDEX TERMS: Methods & Equipment
Fast Flow Q Sepharose anion exchange chromatography: chromatographic techniques, separation method; **atomic force microscopy**: **microscopy** method, **microscopy**: CB
REGISTRY NUMBER: 25104-18-1Q (POLYLYSINE)
38000-06-5Q (POLYLYSINE)

L3 ANSWER 7 OF 16 BIOSIS COPYRIGHT 2001 BIOSIS
ACCESSION NUMBER: 1999:187181 BIOSIS
DOCUMENT NUMBER: PREV199900187181
TITLE: Activity of a single [illegible] **atomic force microscopy**.
AUTHOR(S): Takeuchi, M. (1); Okada, T. (1)
CORPORATE SOURCE: (1) Joint Research Center for Atom Technology c/o NAIR, 1-1-4 Higashi, Tsukuba, Ibaraki, 305-0046 Japan
SOURCE: Biophysical Journal, (Jan., 1999) Vol. 76, No. 1 PART 2, pp. A132.
Meeting Info.: Forty-third Annual Meeting of the Biophysical Society Baltimore, Maryland, USA February

13-17, 1999
ISSN: 0006-3495.

DOCUMENT TYPE: Conference
LANGUAGE: English
CONCEPT CODE: Biochemical Studies - General *10060
Biochemical Methods - General *10050
Enzymes - General and Comparative Studies; Coenzymes *10802
General Biology - Symposia, Transactions and Proceedings of Conferences, Congresses, Review Annuals *00520
INDEX TERMS: Major Concepts
Enzymology (Biochemistry and Molecular Biophysics); Methods and Techniques
INDEX TERMS: Chemicals & Biochemicals
exonuclease: activity; **DNA**
INDEX TERMS: Methods & Equipment
atomic force microscopy: microscopy method, **microscopy**: CB
INDEX TERMS: Miscellaneous Descriptors
enzyme kinetics; protein-**nucleic** acid interactions; Meeting Abstract; Meeting Poster
REGISTRY NUMBER: 37228-74-3 (EXONUCLEASE)

L3 ANSWER 8 OF 16 BIOSIS COPYRIGHT 2001 BIOSIS
ACCESSION NUMBER: 1998:256680 BIOSIS
DOCUMENT NUMBER: PREV199800256680
TITLE: Novel vectors for gene delivery formed by self-assembly of **DNA** with poly(L-lysine) grafted with hydrophilic polymers.
AUTHOR(S): Toncheva, Veska; Wolfert, Margreet A.; Dash, Philip R.; Oupicky, David; Ulbrich, Karel; Seymour, Leonard W. (1); Schacht, Etienne H.
CORPORATE SOURCE: (1) CRC Inst. Cancer Studies, Univ. Birmingham, Birmingham B15 2TA UK
SOURCE: Biochimica et Biophysica Acta, (May 8, 1998) Vol. 138, No. 3, pp. 354-368.
ISSN: 0006-3002.
DOCUMENT TYPE: Article
LANGUAGE: English
ABSTRACT:
Complexes formed between **DNA** and cationic polymers are attracting increasing attention as novel synthetic vectors for delivery of genes. We are trying to improve biological properties of such complexes by oriented self-assembly of **DNA** with cationic-hydrophilic block copolymers, designed to enshroud the complex within a protective hydrophilic polymer corona. Poly(L-lysine) (pLL) grafted with range of hydrophilic polymer blocks, including poly(ethylene glycol) (pEG), dextran and poly(N-(2-hydroxypropyl)methacrylamide) (pHPMA), shows efficient binding to **DNA** and mediates particle self-assembly and inhibition of ethidium bromide/***DNA*** fluorescence. The complexes formed are discrete and typically about 100 nm diameter, viewed by **atomic force microscopy**. Surface charges are slightly shielded by the presence of the hydrophilic polymer, and complexes generally show decreased cytotoxicity compared with simple pLL/**DNA** complexes. pEG-containing complexes show increased transfection activity against cells in vitro. Complexes formed with [illegible] conjugates showed greater aqueous solubility than simple pLL/**DNA** complexes, particularly at charge neutrality. These materials appear to have the ability to regulate the physicochemical and biological properties of polycation/**DNA** complexes, and should find important applications in packaging of **nucleic** acids for specific biological applications.
CONCEPT CODE: Genetics and Cytogenetics - General *03502
Microscopy Techniques - Electron Microscopy *01058
Biochemical Studies - Nucleic Acids, Purines and Pyrimidines *10062

Biochemical Studies - General *10060
INDEX TERMS: Major Concepts
Biochemistry and Molecular Biophysics
INDEX TERMS: Chemicals & Biochemicals
hydrophilic polymers; poly(L-lysine); **DNA**: self-assembly
INDEX TERMS: Methods & Equipment
atomic force microscopy: analytical method
INDEX TERMS: Miscellaneous Descriptors
gene delivery: novel vectors
REGISTRY NUMBER: 25104-18-1Q (POLY(L-LYSINE))
38000-06-5Q (POLY(L-LYSINE))

L3 ANSWER 9 OF 16 BIOSIS COPYRIGHT 2001 BIOSIS
ACCESSION NUMBER: 1998:256659 BIOSIS
DOCUMENT NUMBER: PREV199800256659
TITLE: Analysis of various sequence-specific triplexes by electron and **atomic force** microscopies.
AUTHOR(S): Cherny, Dimitry I. (1); Fourcade, Alain; Svinarchuk, Fedro; Nielsen, Peter E.; Malvy, Claude; Delain, Etienne
CORPORATE SOURCE: (1) Lab. Microscopie Cellulaire Moleculaire, URA 147, CNRS, Inst. Gustave-Roussy, rue Camille Desmoulins, F-94805 Villejuif France
SOURCE: Biophysical Journal, (Feb., 1998) Vol. 74, No. 2 PART 1, pp. 1015-1023.
ISSN: 0006-3495.
DOCUMENT TYPE: Article
LANGUAGE: English
ABSTRACT:
Sequence-specific interactions of 20-mer G,A-containing triple helix-forming oligonucleotides (TFOs) and bis-PNAs (peptide **nucleic** acids) with double-stranded **DNA** was visualized by electron (EM) and ***atomic*** **force** (AFM) microscopies. Triplexes formed by biotinylated TFOs are easily detected by both EM and AFM in which streptavidin is a marker. AFM images of the unlabeled triplex within a long plasmid ***DNA*** show a apprx0.4-nm height increment of the double helix within the target site position. TFOs conjugated to a 74-nt-long oligonucleotide forming a 33-bp-long hairpin form extremely stable triplexes with the target site that are readily imaged by both EM and AFM as protruding **DNA**. The short duplex protrudes in a perpendicular direction relative to the double helix axis, either in the plane of the support or out of it. In the latter case, the apparent height of the protrusion is apprx 1.5 nm, when that of the triplex site is increased by 0.3-0.4 nm. Triplex formation by bis-PNA, [illegible] decamers of PNA are connected via a flexible linker, causes deformations of the double helix at the target site, which is readily detected as kinks by both EM and AFM. Moreover, AFM shows that these kinks are often accompanied by an increase in the **DNA** apparent height of apprx 35%. This work shows the first direct visualization of sequence-specific interaction of TFOs and PNAs, with their target sequences within long plasmid DNAs, through the measurements of the apparent height of the **DNA** double helix by AFM.
CONCEPT CODE: Genetics and Cytogenetics - General *03502
Microscopy Techniques - Electron Microscopy *01058
Biochemical Methods - Nucleic Acids, Purines and Pyrimidines *10052
Biochemical Methods - Proteins, Peptides and Amino Acids *10054
Biochemical Studies - Nucleic Acids, Purines and Pyrimidines *10062
Biochemical Studies - Proteins, Peptides and Amino Acids *10064
Biophysics - Molecular Properties and Macromolecules *10506
INDEX TERMS: Major Concepts

Methods and Techniques; Molecular Genetics (Biochemistry and Molecular Biophysics)

INDEX TERMS: Chemicals & Biochemicals
bis-peptide **nucleic** acid: **DNA** interaction; double-stranded **DNA**; triple helix-forming oligonucleotide: **DNA** interaction

INDEX TERMS: Methods & Equipment
atomic force microscopy: analytical method; electron **microscopy**: analytical method

L3 ANSWER 10 OF 16 BIOSIS COPYRIGHT 2001 BIOSIS

ACCESSION NUMBER: 1998:221880 BIOSIS

DOCUMENT NUMBER: PREV199800221880

TITLE: Study of the interaction of **DNA** with cisplatin and other Pd(II) and Pt(II) complexes by **atomic force microscopy**.

AUTHOR(S): Onoa, G. Bibiana; Cervantes, Gemma; Moreno, Virtudes (1); Prieto, M. Jose

CORPORATE SOURCE: (1) Dep. Quim. Inorg., Univ. Barcelona, Diagonal 647, 08028-Barcelona Spain

SOURCE: Nucleic Acids Research, (March 15, 1998) Vol. 26, No. 6, pp. 1473-1480.
ISSN: 0305-1048.

DOCUMENT TYPE: Article

LANGUAGE: English

ABSTRACT:

Modifications in the structure of a 260 bp **DNA** (hlyM) fragment from Escherichia coli caused by interaction with Pd(II) and Pt(II) complexes were studied. Cisplatin and transplatin (cis- and trans-PtCl2(NH3)2 respectively), Pt2Cl2(Spym)4 (SPYM = 2-mercaptopyrimidine anion), Pd-famotidine and Pt-famotidine were incubated with **DNA** for 24 h at 37degreeC and then observed with an **atomic force** microscope. **Atomic** ***force*** **microscopy** (AFM) provides the opportunity for nanometer resolution in research on the interaction between **nucleic** acids and metal complexes. The complexes induced noticeable changes in **DNA** topography according to their different characteristics and structure. In the case of cisplatin a shortening in **DNA** strands was observed. Transplatin and Pt2Cl2(SPYM)4 caused shortening and compaction, whilst an aggregation of two strands was observed for the Pt-famotidine compound but not for the Pd-famotidine compound or the metal-free famotidine.

CONCEPT CODE: Biochemical Methods - Nucleic Acids, Purines and Pyrimidines *10052
Microscopy Techniques - General and Special Techniques *01052
Biochemical Methods - Minerals *10059
Biophysics - Molecular Properties and Macromolecules *10506

INDEX TERMS: Major Concepts
Biochemistry and Molecular Biophysics; Methods and Techniques

INDEX TERMS: Chemicals & Biochemicals
cisplatin: Roy[illegible]ton, quantitative analysis; hlyM gene; palladium (II) ion: quantitative analysis; platinum ion: quantitative analysis; transplatin: Roy[illegible]ton, quantitative analysis; **DNA**: quantitative analysis

INDEX TERMS: Methods & Equipment
atomic force microscopy: **microscopy** method; polymerase chain reaction: amplification method, sequencing techniques; GeneAmp PCR system 2400: Perkin-Elmer Cetus, equipment; Nanoscope III Multimode AFM: Digital Instrumentals Inc, equipment

INDEX TERMS: Miscellaneous Descriptors
nucleic acid-metal interaction

REGISTRY NUMBER: 15663-27-1 (CISPLATIN)
16065-88-6 (PALLADIUM (II))
22542-10-5 (PLATINUM (II))
14913-33-8 (TRANSPLATIN)

L3 ANSWER 11 OF 16 BIOSIS COPYRIGHT 2001 BIOSIS
ACCESSION NUMBER: 1997:243950 BIOSIS
DOCUMENT NUMBER: PREV199799543153
TITLE: **DNA** looping by Ku and the **DNA**-dependent protein kinase.
AUTHOR(S): Cary, Robert B.; Peterson, Scott R.; Wang, Jinting; Bear, David G.; Bradbury, E. Morton; Chen, David J. (1)
CORPORATE SOURCE: (1) Life Sci. Div., Los Alamos Natl. Lab., Mail Stop M888, Los Alamos, NM 87545 USA
SOURCE: Proceedings of the National Academy of Sciences of the United States of America, (1997) Vol. 94, No. 9, pp. 4267-4272.
ISSN: 0027-8424.
DOCUMENT TYPE: Article
LANGUAGE: English
ABSTRACT:
The **DNA**-dependent protein kinase (**DNA**-PK) is required for ***DNA*** double-strand break (DSB) repair and immunoglobulin gene rearrangement and may play a role in the regulation of transcription. The ***DNA*** -PK holoenzyme is composed of three polypeptide subunits: the ***DNA*** binding Ku70/86 heterodimer and an apprxeq 460-kDa catalytic subunit (**DNA**-PKcs). **DNA**-PK has been hypothesized to assemble at **DNA** DSBs and play structural as well as signal transduction roles in DSB repair. Recent advances in **atomic** ***force*** **microscopy** (AFM) have resulted in a technology capable of producing high resolution images of native protein and proteinnucleic acid complexes without staining or metal coating. The AFM provides a rapid and direct means of probing the protein-**nucleic** acid interactions responsible for **DNA** repair and genetic regulation. Here we have employed AFM as well as electron **microscopy** to visualize Ku and ***DNA*** -PK in association with **DNA**. A significant number of ***DNA*** molecules formed loops in the presence of Ku. **DNA** looping appeared to be sequence-independent and unaffected by the presence of ***DNA*** -PKcs. Gel filtration of Ku in the absence and the presence of ***DNA*** indicates that Ku does not form nonspecific aggregates. We conclude that, when bound to **DNA**, Ku is capable of self-association. These findings suggest that Ku binding at **DNA** DSBs will result in Ku self-association and a physical tethering of the broken **DNA** ends.
CONCEPT CODE: Biochemical Studies - Nucleic Acids, Purines and Pyrimidines *10062
Biochemical Studies - Proteins, Peptides and Amino Acids *10064
Biophysics - Molecular Properties and Macromolecules *10506
Enzymes - Physiological Studies *10808
INDEX TERMS: Major Concepts
Biochemistry and Molecular Biophysics; Enzymology (Biochemistry and Molecular Biophysics)
INDEX TERMS: Chemicals & Biochemicals
PROTEIN KINASE
INDEX TERMS: Miscellaneous Descriptors
BIOCHEMISTRY AND BIOPHYSICS; **DNA**; **DNA** -DEPENDENT PROTEIN KINASE; KU70/86 HETERODIMER; LOOPING
REGISTRY NUMBER: 9026-43-1 (PROTEIN KINASE)

L3 ANSWER 12 OF 16 BIOSIS COPYRIGHT 2001 BIOSIS
ACCESSION NUMBER: 1996:150019 BIOSIS
DOCUMENT NUMBER: PREV199698722154
TITLE: **Atomic force microscopy** o:

long and short double-stranded, single-stranded and triple-stranded **nucleic** acids.

AUTHOR(S): Hansma, Helen G. (1); Revenko, Irene; Kim, Kery; Laney, Daniel E.

CORPORATE SOURCE: (1) Dep. Physics, Univ. California, Santa Barbara CA 93106 USA

SOURCE: Nucleic Acids Research, (1996) Vol. 24, No. 4, pp. 713-720. ISSN: 0305-1048.

DOCUMENT TYPE: Article

LANGUAGE: English

ABSTRACT:

Atomic force microscopy (AFM, also called scanning **force microscopy**) is proving to be a useful technique for imaging **DNA**. Thus it is important to push the limits of AFM imaging in order to explore both what types of **DNA** can be reliably imaged and identified and also what substrates and methods of sample preparation are suitable. The following advances in AFM of **DNA** are presented here. (i) **DNA** molecules as short as 25 bases can be seen by AFM. The short single-stranded DNAs imaged here (25 and 50 bases long) appeared globular in the AFM, perhaps because they are all capable of intramolecular base pairing and because the DNAs were in a Mg(II) buffer, which facilitates intramolecular cross-bridging. (ii) AFM images in air of short double-stranded ***DNA*** molecules, 100-200 bp, gave lengths consistent with A-**DNA**. (iii) AFM images of poly(A) show both short bent lumpy molecules with an apparent persistence length of 40 nm and long straight molecules with an apparent persistence length of 600 nm. For comparison, the apparent persistence length for double-stranded **DNA** from vphi-X-174 under the same conditions was 80 nm. (iv) Structures believed to be triple-stranded ***DNA*** were seen in samples of poly(dA) cntdot poly(dT) and poly(dG) cntdot poly(dC). These structures were twice as high as double-stranded ***DNA*** and the same width. (v) Entire molecules of lambda **DNA**, apprx 16 mu-m long, were imaged clearly in overlapping states. [illegible] ***DNA*** was imaged on oxidized silicon, although less clearly than on mica.

CONCEPT CODE: Microscopy Techniques - General and Special Techniques 01052
Biochemical Methods - Nucleic Acids, Purines and Pyrimidines *10052
Biochemical Studies - Nucleic Acids, Purines and Pyrimidines *10062
Biophysics - General Biophysical Techniques *10504
Biophysics - Molecular Properties and Macromolecules *10506
Physiology and Biochemistry of Bacteria *31000
Genetics of Bacteria and Viruses *31500

BIOSYSTEMATIC CODE: Bacteria - General Unspecified *05000

INDEX TERMS: Major Concepts
Biochemistry and Molecular Biophysics; Genetics; Methods and Techniques; Physiology

INDEX TERMS: Miscellaneous Descriptors
CROSS-BRIDGING; **DNA** IMAGING; INTRAMOLECULAR BASE PAIRING; LAMBDA-**DNA**; PLASMID **DNA**; SCANNING **FORCE MICROSCOPY**

ORGANISM: Super Taxa
Bacteria - General Unspecified: Eubacteria, Bacteria

ORGANISM: Organism Name
bacteria (Bacteria - General Unspecified)

ORGANISM: Organism Superterms
bacteria; eubacteria; microorganisms

L3 ANSWER 13 OF 16 BIOSIS COPYRIGHT 2001 BIOSIS

ACCESSION NUMBER: 1996:125528 BIOSIS

DOCUMENT NUMBER: PREV199698697663

TITLE: Scanning probe **microscopy** in microbiology.

AUTHOR(S): Firtel, M.,; Beveridge, T. J. (1)

CORPORATE SOURCE: (1) Department Microbiology, Faculty Medicine, [illegible] Toronto, Toronto, ON M5S 1A8 Canada

SOURCE: Micron, (1995) Vol. 26, No. 4, pp. 347-362.
ISSN: 0968-4328.

DOCUMENT TYPE: General Review
LANGUAGE: English
CONCEPT CODE: Microscopy Techniques - General and Special Techniques *01052
Biochemical Methods - Nucleic Acids, Purines and Pyrimidines *10052
Biochemical Studies - Nucleic Acids, Purines and Pyrimidines 10062
Biophysics - Molecular Properties and Macromolecules *10506
Anatomy and Histology, General and Comparative - Microscopic and Ultramicroscopic Anatomy *11108
Metabolism - Nucleic Acids, Purines and Pyrimidines *13014
Morphology and Cytology of Bacteria *30500
Physiology and Biochemistry of Bacteria *31000
Genetics of Bacteria and Viruses *31500
Microbiological Apparatus, Methods and Media *32000
Microbiological Ultrastructure *32300
Virology - Bacteriophage *33504
Virology - Animal Host Viruses *33506
Virology - Plant Host Viruses *33508
BIOSYSTEMATIC CODE: Animal Viruses - General 02600
Bacterial Viruses - General 02700
Plant Viruses - General 02800
Enterobacteriaceae 06702
Deinococcaceae 07701
Methanomicrobiaceae 09531
Halobacteriaceae *09711
INDEX TERMS: Major Concepts
Biochemistry and Molecular Biophysics; Cell Biology; Genetics; Metabolism; Methods and Techniques; Microbiology; Morphology; Physiology
INDEX TERMS: Miscellaneous Descriptors
ANALYTICAL METHOD; **ATOMIC FORCE MICROSCOPY**; BACTERIAL SURFACE LAYER; BACTERIOPHAGE SURFACE LAYER; **DNA**; MICROBIAL CELL VISCOELASTICITY; **NUCLEIC** ACID; SCANNING TUNNELLING **MICROSCOPY**; SURFACE TOPOGRAPHY; VIRAL SURFACE LAYER
ORGANISM: Super Taxa
Animal Viruses - General: Viruses; Bacterial Viruses - General: Viruses; Deinococcaceae: Eubacteria, Bacteria; Enterobacteriaceae: Eubacteria, Bacteria; Halobacteriaceae: Archaeobacteria, Bacteria; Methanomicrobiaceae: Archaeobacteria, Bacteria; Plant Viruses - General: Viruses
ORGANISM: Organism Name
animal viruses (Animal Viruses - General); bacterial viruses (Bacterial Viruses - General); Deinococcus radiodurans (Deinococcaceae); Escherichia coli (Enterobacteriaceae); Halobacterium (Halobacteriaceae); Methanospirillum hungatei (Methanomicrobiaceae); Plant Viruses (Plant Viruses - General)
ORGANISM: Organism Superterms
archaeobacteria; bacteria; eubacteria; microorganisms; viruses

L3 ANSWER 14 OF 16 BIOSIS COPYRIGHT 2001 BIOSIS
ACCESSION NUMBER: 1995:201818 BIOSIS
DOCUMENT NUMBER: PREV199599216118
TITLE: A new **DNA** nanostructure, the G-wire, imaged by

scanning probe **microscopy**.

AUTHOR(S): Marsh, Thomas C.; Vesenka, James; Henderson, Eric (1)
CORPORATE SOURCE: (1) Dep. Zool. Genet., 2112 Mol. Biol. Build., Iowa State Univ., Ames, IA 50011 USA
SOURCE: Nucleic Acids Research, (1995) Vol. 23, No. 4, pp. 696-[illegible].
ISSN: 0305-1048.
DOCUMENT TYPE: Article
LANGUAGE: English
ABSTRACT:
G-**DNA** is a polymorphic family of quadruple helical **nucleic** acid structures containing guanine tetrad motifs (G-quartets; Williamson, J.R., Raghuraman, M.K. and Cech, TR. (1989) Cell 59,871-880; Williamson, J.R. (1993) Proc. Natl. Acad Sci. USA 90, 3124-3124). Guanine rich oligonucleotides that are self-complimentary, as found in many telomeric G-strand repeat sequences, form G-**DNA** In the presence of monovalent and/or divalent metal cations. In this report we use the **atomic force** microscope (AFM) to explore the structural characteristics of long, linear polymers formed by the telomeric oligonucleotide d(GGGG TTGGGG) in the presence of specific metal cations. In the AFM these polymers, termed G-wires, appear as filaments whose height and length are determined by the metal ions present during the self-assembly process. The highly ordered, controllable self-assembly of G-wires could provide a basis for developing advanced biomaterials.
CONCEPT CODE: Microscopy Techniques - Electron Microscopy *01058
Biochemical Methods - Nucleic Acids, Purines and Pyrimidines 10052
Biochemical Studies - Nucleic Acids, Purines and Pyrimidines *10062
Biophysics - General Biophysical Techniques 10504
Biophysics - Molecular Properties and Macromolecules *10506
INDEX TERMS: Major Concepts
Biochemistry and Molecular Biophysics; Methods and Techniques
INDEX TERMS: Miscellaneous Descriptors
ANALYTICAL METHOD; **ATOMIC FORCE** MICROSCOPE; ION BIOSENSOR; OLIGONUCLEOTIDE

L3 ANSWER 15 OF 16 BIOSIS COPYRIGHT 2001 BIOSIS
ACCESSION NUMBER: 1994:327879 BIOSIS
DOCUMENT NUMBER: PREV199497340879
TITLE: **Atomic force microscopy** in basic and applied **nucleic** acid research.
AUTHOR(S): Henderson, Eric
CORPORATE SOURCE: Zool. and Genetics, Iowa State Univ., Ames, IA 50011 USA
SOURCE: Clinical Chemistry, (1994) Vol. 40, No. 4, pp. 653.
Meeting Info.: 8th San Diego Conference on Beyond DNA Probes San Diego, California, USA November 18-20, 1993
ISSN: 0009-9147.
DOCUMENT TYPE: Conference
LANGUAGE: English
CONCEPT CODE: General Biology - Symposia, Transactions and Proceedings of Conferences, Congresses, Review Annuals [illegible]
Microscopy Techniques - General and Special Techniques *01052
Genetics and Cytogenetics - General *03502
Biochemical Methods - Nucleic Acids, Purines and Pyrimidines *10052
Biochemical Studies - Nucleic Acids, Purines and Pyrimidines *10062
Biophysics - General Biophysical Techniques *10504
Biophysics - Molecular Properties and Macromolecules *10506
BIOSYSTEMATIC CODE: *00500
INDEX TERMS: Major Concepts

Biochemistry and Molecular Biophysics; Genetics; Methods and Techniques

INDEX TERMS: Miscellaneous Descriptors
DNA TOPOGRAPHY; MEETING ABSTRACT; VISUALIZATION METHOD

ORGANISM: Organism Name
organisms (Organisms - Unspecified)

L3 ANSWER 16 OF 16 BIOSIS COPYRIGHT 2001 BIOSIS

ACCESSION NUMBER: 1992:156807 BIOSIS

DOCUMENT NUMBER: BR42:73007

TITLE: **ATOMIC FORCE MICROSCOPY**
IMAGING OF LARGE DOUBLE STRANDED **DNA** MOLECULES.

AUTHOR(S): LYUBCHENKO Y L; GALL A A; SHLYAKHTENKO L S; HARRINGTON R E; LINDSAY S M

CORPORATE SOURCE: DEP. BIOCHEMISTRY, UNIV. NEVADA RENO, RENO, NV 89557.

SOURCE: JOINT MEETING OF THE AMERICAN SOCIETY FOR BIOCHEMISTRY AND MOLECULAR BIOLOGY/BIOPHYSICAL SOCIETY, HOUSTON, TEXAS, USA, FEBRUARY 9-13, 1992. FASEB (FED AM SOC EXP BIOL) J, 1992 6 (1), A149.
CODEN: FAJOEC. ISSN: 0892-6638.

DOCUMENT TYPE: Conference

FILE SEGMENT: BR; OLD

LANGUAGE: English

CONCEPT CODE: General Biology - Symposia, Transactions and Proceedings of Conferences, Congresses, Review Annuals 00520
Genetics and Cytogenetics - General *03502
Biochemical Studies - Nucleic Acids, Purines and Pyrimidines *10062
Biophysics - Molecular Properties and Macromolecules *10506

INDEX TERMS: Miscellaneous Descriptors
ABSTRACT GENOMIC MAPPING **NUCLEIC** ACID-PROTEIN COMPLEXES

L3 ANSWER 1 OF 16 BIOSIS COPYRIGHT 2001 BIOSIS
ACCESSION NUMBER: 2000:544893 BIOSIS
DOCUMENT NUMBER: PREV200000544893
TITLE: The effect of super-oxidized water on Escherichia coli.
AUTHOR(S): Zinkevich, V. (1); Beech, I. B.; Tapper, R.; Bogdarina, I.
CORPORATE SOURCE: (1) School of Pharmacy and Biomedical Sciences, University of Portsmouth, White Swan Road, St. Michael's Building, Portsmouth, PO1 2DT UK
SOURCE: Journal of Hospital Infection, (October, 2000) Vol. 46, No. 2, pp. 153-156. print.
ISSN: 0195-6701.
DOCUMENT TYPE: Article
LANGUAGE: English
SUMMARY LANGUAGE: English
ABSTRACT:
The mechanism of action of Sterilox, a non-toxic liquid biocide produced by electrolysis of a dilute saline solution, upon planktonic cells of Escherichia coli JM109 was investigated using protein and **nucleic** acid analysis. The results revealed total destruction of chromosomal and plasmid **DNA**, RNA and proteins of E. coli within 5 min of exposure. Our earlier investigation conducted using **atomic force** ***microscopy*** imaging revealed swelling and rupture of E. coli cells with release of cytoplasm. We propose that the biocidal properties of Sterilox are due to its effect upon constituents of the bacterial cell including proteins and **nucleic** acids.
CONCEPT CODE: Physiology and Biochemistry of Bacteria *31000
Biochemical Studies - Nucleic Acids, Purines and Pyrimidines *10062
Biochemical Studies - Proteins, Peptides and Amino Acids *10064
Public Health: Environmental Health - Sewage Disposal and Sanitary Measures *37014
Pest Control, General; Pesticides; Herbicides *54600
BIOSYSTEMATIC CODE: Enterobacteriaceae 06702
INDEX TERMS: Major Concepts
Sanitation
INDEX TERMS: Chemicals & Biochemicals
Sterilox: biocide; plasmid **DNA**; plasmid RNA; proteins; super-oxidized water
INDEX TERMS: Methods & Equipment
electrolysis: synthetic method; **nucleic** acid analysis: analytical method; protein analysis: analytical method
ORGANISM: Super Taxa
Enterobacteriaceae: Facultatively Anaerobic Gram-Negative Rods, Eubacteria, Bacteria, Microorganisms; Hominidae: Primates, Mammalia, Vertebrata, Chordata, Animalia
ORGANISM: Organism Name
Escherichia coli (Enterobacteriaceae): pathogen, strain-JM109; human (Hominidae): patient
ORGANISM: Organism Superterms
Animals; Bacteria; Chordates; Eubacteria; Humans; Mammals; Microorganisms; Primates; Vertebrates

L3 ANSWER 2 OF 16 BIOSIS COPYRIGHT 2001 BIOSIS
ACCESSION NUMBER: 2000:497584 BIOSIS
DOCUMENT NUMBER: PREV200000497705
TITLE: Near field microscopies: From isolated molecules to living cells.
AUTHOR(S): Delain, E. (1); Michel, D. (1); Le Grimellec, Ch.
CORPORATE SOURCE: (1) Laboratoire de Microscopie Moleculaire et Cellulaire/CNRS UMR 8532, Institut Gustave Roussy, Rue Camille Desmoulins, Villejuif France
SOURCE: Morphologie, (Juin, 2000) Vol. 84, No. 265, pp. 25-30.

print.
ISSN: 1286-0115.
DOCUMENT TYPE: Article
LANGUAGE: French
SUMMARY LANGUAGE: English; French
ABSTRACT:
Near field (or scanning probe) **microscopy** is a recent technology which, owing to the huge amount of publications, is becoming a reference method in molecular and cellular imaging. These microscopies consist in the scanning of the sample, line by line, with a very tiny tip and thus providing informations on its surface down to the nanometer scale. These methods gather scanning tunelling **microscopy** (STM), which measures a current between the tip and the specimen support, **atomic force** ***microscopy*** (AFM), which measures the repulsive and attractive forces of the tip in contact or very close to the specimen, and scanning near field optical microscopies (SNOM), for which a glass tip allows to catch light signals. **Atomic force microscopy**, which allows the observation of specimens in air or physiological conditions environments, is presently dominant in biology, in complementarity with the classical optical and electron microscopies, which by the way, have also shown considerable improvements during the last years. The complementarity of these microscopies is due to their very different basic principles, which provide them various possibilities and limits. The biological applications of STM is limited by the need of conducting samples, but the different models of SNOM, often still is development, allow to consider very interesting applications, particularly for detecting very faint and tiny fluorescence signals. Different examples will be given concerning the visualization by AFM of isolated **DNA** molecules, naked or associated with proteins, the observation of intact or decondensed chromosomes, as well as living cells. One of the originality of AFM is its capacity to observed objects in a wide range of enlargements, with fields from a few hundred of nanometers to several micrometers.
CONCEPT CODE: Cytology and Cytochemistry - General *02502
Biochemical Studies - General *10060
Biochemical Studies - Nucleic Acids, Purines and Pyrimidines *10062
Biochemical Studies - Proteins, Peptides and Amino Acids *10064
INDEX TERMS: Major Concepts
Biochemistry and Molecular Biophysics; Cell Biology; Methods and Techniques
INDEX TERMS: Parts, Structures, & Systems of Organisms
cells: near field microscopic study
INDEX TERMS: Chemicals & Biochemicals
double stranded **DNA**: microscopic study; **nucleic** acids: microscopic study; proteins: microscopic study
INDEX TERMS: Methods & Equipment
scanning near field optical **microscopy**: analytical method; scanning probe **microscopy** [near field **microscopy**]: analytical method
ORGANISM: Super Taxa
Organisms
ORGANISM: Organism Name
organism (Organisms)

L3 ANSWER 3 OF 16 BIOSIS COPYRIGHT 2001 BIOSIS
ACCESSION NUMBER: 2000:309262 BIOSIS
DOCUMENT NUMBER: PREV200000309262
TITLE: A dimer as a building block in assembling RNA: A hexamer that gears bacterial virus phi29 **DNA** -translocating machinery.
AUTHOR(S): Chen, Chaoping; Sheng, Sitong; Shao, Zhifeng; Guo, Peixuan
SOURCE: Journal of Biological Chemistry, (June 9, 2000) Vol. 275, No. 23, pp. 17510-17516. print.

ISSN: 0021-9258.
DOCUMENT TYPE: Article
LANGUAGE: English
SUMMARY LANGUAGE: English
ABSTRACT:
Six RNA (pRNA) molecules form a hexamer, via hand-in-hand interaction, to gear bacterial virus phi29 **DNA** translocation machinery. Here we report the pathway and the conditions for the hexamer formation. Stable pRNA dimers and trimers were assembled in solution, isolated from native gels, and separated by sedimentation, providing a model system for the study of RNA dimers and trimers in a protein-free environment. Cryoatomic **force microscopy** revealed that monomers displayed a check-mark shaped outline, dimers exhibited an elongated shape, and trimers formed a triangle. Dimerization of pRNA was promoted by a variety of cations including spermidine, whereas procapsid binding and **DNA** packaging required specific divalent cations, including Mg2+, Ca2+, and Mn2+. Both the tandem and fused pRNA dimers with complementary loops designed to form even-numbered rings were active in ***DNA*** packaging, whereas those without complementary loops were inactive. We conclude that dimers are the building blocks of the hexamer, and the pathway of building a hexamer is: dimer fwdarw tetramer fwdarw hexamer. The Hill coefficient of 2.5 suggests that there are three binding sites with cooperative binding on the surface of the procapsid. The two interacting loops played a key role in recruiting the incoming dimer, whereas the procapsid served as the foundation for hexamer assembly.
CONCEPT CODE: Biochemical Studies - Nucleic Acids, Purines and Pyrimidines *10062
Methods, Materials and Apparatus, General - Laboratory Methods *01004
Virology - Animal Host Viruses *33506
Biochemical Studies - Minerals *10069
INDEX TERMS: Major Concepts
Biochemistry and Molecular Biophysics; Methods and Techniques
INDEX TERMS: Chemicals & Biochemicals
DNA-translocating machinery; RNA: assay, isolation, separation, synthesis; calcium (II); magnesium (II); manganese (II)
INDEX TERMS: Methods & Equipment
PAGE [polyacrylamide gel electrophoresis]: gel electrophoresis, isolation method; RNA binding assay: analytical method, binding assays; RNA synthesis: **nucleic** acid synthesis, synthetic method; cryo-**atomic force microscopy** [cryo-AFM]: **microscopy** method, **microscopy** : CB; dimer binding competition assay: Analysis/Characterization Techniques: CB, analytical method; sucrose gradient sedimentation: Extraction, isolation, Purification and Separation Techniques, separation method; virion assembly assay: Analysis/Characterization Techniques: CB, analytical method
ORGANISM: Super Taxa
Podoviridae: Bacterial Viruses, Viruses, Microorganisms
ORGANISM: Organism Name
phi29 (Podoviridae)
ORGANISM: Organism Superterms
Bacterial Viruses; Microorganisms; Viruses
REGISTRY NUMBER: 14127-61-8 (CALCIUM (II))
22537-22-0 (MAGNESIUM (II))
16397-91-4 (MANGANESE (II))

L3 ANSWER 4 OF 16 BIOSIS COPYRIGHT 2001 BIOSIS
ACCESSION NUMBER: 2000:246496 BIOSIS
DOCUMENT NUMBER: PREV200000246496
TITLE: PNA-dependent gene chemistry: Stable coupling of peptides

and oligonucleotides to plasmid **DNA**.

AUTHOR(S): Zelphati, O.; Liang, X.; Nguyen, C.; Barlow, S.; Sheng, S.; Shao, Z.; Felgner, P. L. (1)

CORPORATE SOURCE: (1) Gene Therapy Systems, 10190 Telesis Court, San Diego, CA, 92121 USA

SOURCE: Biotechniques, (Feb., 2000) Vol. 28, No. 2, pp. 304-316. ISSN: 0736-6205.

DOCUMENT TYPE: Article

LANGUAGE: English

SUMMARY LANGUAGE: English

ABSTRACT:

Two approaches are described for stably conjugating peptides, proteins and oligonucleotides onto plasmid **DNA**. Both methods use a peptide ***nucleic*** acid (PNA) clamp, which binds irreversibly and specifically to a binding site cloned into the plasmid. The first approach uses a biotin-conjugated PNA clamp that can be used to introduce functional biotin groups onto the plasmid to which streptavidin can bind. **Atomic** ***force*** **microscopy** images of linearized plasmid show streptavidin localized at the predicted PNA binding site on the **DNA** strand. Peptides and oligonucleotides containing free thiol groups were conjugated to maleimide streptavidin, and these streptavidin conjugates were bound to the biotin-PNA-labeled plasmid. In this way, peptides and oligonucleotides could be brought into stable association with the plasmid. A second approach used a maleimide-conjugated PNA clamp. Methods are described for conjugating thiolated peptides and oligonucleotides directly to the maleimide-PNA-**DNA** hybrid. This straightforward technology offers an easy approach to introduce functional groups onto plasmid **DNA** without disturbing its transcriptional activity.

CONCEPT CODE: Biochemical Methods - Nucleic Acids, Purines and Pyrimidines *10052
Biochemical Studies - Proteins, Peptides and Amino Acids *10064
Biophysics - General Biophysical Techniques *10504
Genetics of Bacteria and Viruses *31500

INDEX TERMS: Major Concepts
Molecular Genetics (Biochemistry and Molecular Biophysics); Methods and Techniques

INDEX TERMS: Chemicals & Biochemicals
oligonucleotides; peptide **nucleic** acid; peptides; plasmid **DNA**

INDEX TERMS: Methods & Equipment
ATTO-TAG labeling kit: Molecular Probes, equipment; agarose gel electrophoresis: analytical method, gel electrophoresis; **atomic force** **microscopy**: **microscopy** method, **microscopy**: CB, **microscopy**: CT; transfection: gene expression/vector techniques, genetic method; transmission electron **microscopy**: electron **microscopy**: CB, electron **microscopy**: CT, **microscopy** method

INDEX TERMS: Miscellaneous Descriptors
PNA-dependent gene chemistry

L3 ANSWER 5 OF 16 BIOSIS COPYRIGHT 2001 BIOSIS

ACCESSION NUMBER: 2000:61886 BIOSIS

DOCUMENT NUMBER: PREV200000061886

TITLE: Polymerase activities and RNA structures in the **atomic force** microscope.

AUTHOR(S): Hansma, Helen G. (1); Golan, Roxana; Hsieh, Wan; Daubendiek, Sarah L.; Kool, Eric T.

CORPORATE SOURCE: (1) Department of Physics, University of California, Santa Barbara, Santa Barbara, CA USA

SOURCE: Journal of Structural Biology, (Oct., 1999) Vol. 127, No. 3, pp. 240-247.

ISSN: 1047-8477.
DOCUMENT TYPE: Article
LANGUAGE: English
SUMMARY LANGUAGE: English
ABSTRACT:
The structures of the reaction products are the basis for novel polymerase assays using the **atomic force** microscope (AFM). Polymerases are the enzymes involved in transcription and replication of **DNA**. Rapid semiquantitative estimates of the activity of **DNA** polymerases such as Sequenase, Taq polymerase, and AMV reverse transcriptase and RNA polymerases (RNAP) such as Escherichia coli RNAP were obtained from AFM images of the **nucleic** acids after polymerase reactions. **DNA** polymerases were assayed via replication of the single-stranded PHIX-174 virion. RNAP was assayed via transcription, using a rolling circle **DNA** template that produces long strands of RNA. In some cases, AFM was better than agarose gel electrophoresis for assaying **DNA** polymerase activity, since aggregation prevented the **DNA** from entering the agarose gel. Extended molecules of single-stranded RNA synthesized with the rolling circle ***DNA*** template showed varied conformations and degrees of stretching. Some structural differences were observed between two RNAs-a ribozyme concatamer and an RNA with 90% purines.
CONCEPT CODE: Genetics and Cytogenetics - General *03502
Microscopy Techniques - Electron Microscopy *01058
Biochemical Methods - Nucleic Acids, Purines and Pyrimidines *10052
Biochemical Studies - Nucleic Acids, Purines and Pyrimidines *10062
Replication, Transcription, Translation *10300
Biophysics - Molecular Properties and Macromolecules *10506
Enzymes - Methods *10804
Enzymes - Chemical and Physical *10806
Physiology and Biochemistry of Bacteria *31000
Genetics of Bacteria and Viruses *31500
Virology - General; Methods *33502
BIOSYSTEMATIC CODE: Microviridae 02706
Enterobacteriaceae 06702
INDEX TERMS: Major Concepts
Enzymology (Biochemistry and Molecular Biophysics); Molecular Genetics (Biochemistry and Molecular Biophysics
INDEX TERMS: Chemicals & Biochemicals
AMV reverse transcriptase; **DNA**: rolling circle template; **DNA** polymerase; RNA: structure; RNA polymerase; Taq polymerase
INDEX TERMS: Methods & Equipment
atomic force microscope: laboratory equipment; **atomic force microscopy**: analytical method, **microscopy**: CB, molecular imaging method
ORGANISM: Super Taxa
Enterobacteriaceae: Facultatively Anaerobic Gram-Negative Rods, Eubacteria, Bacteria, Microorganisms; Microviridae: Bacterial Viruses, Viruses, Microorganisms
ORGANISM: Organism Name
Escherichia coli (Enterobacteriaceae); bacteriophage phi-X-174 (Microviridae)
ORGANISM: Organism Superterms
Bacteria; Bacterial Viruses; Eubacteria; Microorganisms; Viruses
REGISTRY NUMBER: 9012-90-2 (**DNA** POLYMERASE)
9014-24-8 (RNA POLYMERASE)

L3 ANSWER 6 OF 16 BIOSIS COPYRIGHT 2001 BIOSIS
ACCESSION NUMBER: 2000:2359 BIOSIS

DOCUMENT NUMBER: PREV200000002359
TITLE: **DNA** toroids: Stages in condensation.
AUTHOR(S): Golan, Roxana; Pietrasanta, Lia I.; Hsieh, Wan; Hansma, Helen G. (1)
CORPORATE SOURCE: (1) Department of Physics, UCSB, Santa Barbara, CA, 93106 USA
SOURCE: Biochemistry, (Oct. 19, 1999) Vol. 38, No. 42, pp. 14069-14076.
ISSN: 0006-2960.
DOCUMENT TYPE: Article
LANGUAGE: English
SUMMARY LANGUAGE: English
ABSTRACT:
The effects of polylysine (PLL) and PLL-asialoorosomucoid (AsOR) on **DNA** condensation have been analyzed by AFM. Different types of condensed ***DNA*** structures were observed, which show a sequence of conformational changes as circular plasmid **DNA** molecules condense progressively. The structures range from circular molecules with the length of the plasmid ***DNA*** to small toroids and short rods with apprx1/6 to 1/8 the contour length of the uncondensed circular **DNA**. Single plasmid molecules of 6800 base pairs (bp) condense into single toroids of apprx110 nm diameter, measured center-to-center. The results are consistent with a model for ***DNA*** condensation in which circular **DNA** molecules fold several times into progressively shorter rods. Structures intermediate between toroids and rods suggest that at least some toroids may form by the opening up of rods as proposed by Dunlap et al. ((1997) **Nucleic** Acids Res. 25, 3095). Toroids and rods formed at lysine:nucleotide ratios of 5:1 and 6:1. This high lys ine: nucleotide ratio is discussed in relation to entropic considerations and the overcharging of macroions. PLL-AsOR is much more effective than PLL alone for condensing **DNA**, because several PLL molecules are attached to a single AsOR molecule, resulting in an increased cation density.
CONCEPT CODE: Genetics and Cytogenetics - General *03502
Microscopy Techniques - General and Special Techniques *01052
Biochemical Methods - General *10050
Biochemical Studies - General *10060
Biophysics - General Biophysical Studies *10502
INDEX TERMS: Major Concepts
Molecular Genetics (Biochemistry and Molecular Biophysics); Methods and Techniques
INDEX TERMS: Chemicals & Biochemicals
DNA toroids: analysis, condensation stages; polylysine: **DNA** condenser; polylysine-asialoorosomucoid: **DNA** condenser
INDEX TERMS: Methods & Equipment
Fast Flow Q Sepharose anion exchange chromatography: chromatographic techniques, separation method; **atomic force microscopy**: **microscopy** method, **microscopy**: CB
REGISTRY NUMBER: 25104-18-1Q (POLYLYSINE)
38000-06-5Q (POLYLYSINE)

L3 ANSWER 7 OF 16 BIOSIS COPYRIGHT 2001 BIOSIS
ACCESSION NUMBER: 1999:187181 BIOSIS
DOCUMENT NUMBER: PREV199900187181
TITLE: Activity of a single exonuclease revealed by **atomic force microscopy**.
AUTHOR(S): Takeuchi, M. (1); Okada, T. (1)
CORPORATE SOURCE: (1) Joint Research Center for Atom Technology c/o NAIR, 1-1-4 Higashi, Tsukuba, Ibaraki, 305-0046 Japan
SOURCE: Biophysical Journal, (Jan., 1999) Vol. 76, No. 1 PART 2, pp. A132.
Meeting Info.: Forty-third Annual Meeting of the Biophysical Society Baltimore, Maryland, USA February

13-17, 1999
ISSN: 0006-3495.
DOCUMENT TYPE: Conference
LANGUAGE: English
CONCEPT CODE: Biochemical Studies - General *10060
Biochemical Methods - General *10050
Enzymes - General and Comparative Studies; Coenzymes *10802
General Biology - Symposia, Transactions and Proceedings of Conferences, Congresses, Review Annuals *00520
INDEX TERMS: Major Concepts
Enzymology (Biochemistry and Molecular Biophysics); Methods and Techniques
INDEX TERMS: Chemicals & Biochemicals
exonuclease: activity; **DNA**
INDEX TERMS: Methods & Equipment
atomic force microscopy: **microscopy** method, **microscopy**: CB
INDEX TERMS: Miscellaneous Descriptors
enzyme kinetics; protein-**nucleic** acid interactions; Meeting Abstract; Meeting Poster
REGISTRY NUMBER: 37228-74-3 (EXONUCLEASE)

L3 ANSWER 8 OF 16 BIOSIS COPYRIGHT 2001 BIOSIS
ACCESSION NUMBER: 1998:256680 BIOSIS
DOCUMENT NUMBER: PREV199800256680
TITLE: Novel vectors for gene delivery formed by self-assembly of **DNA** with poly(L-lysine) grafted with hydrophilic polymers.
AUTHOR(S): Toncheva, Veska; Wolfert, Margreet A.; Dash, Philip R.; Oupicky, David; Ulbrich, Karel; Seymour, Leonard W. (1); Schacht, Etienne H.
CORPORATE SOURCE: (1) CRC Inst. Cancer Studies, Univ. Birmingham, Birmingham B15 2TA UK
SOURCE: Biochimica et Biophysica Acta, (May 8, 1998) Vol. 138, No. 3, pp. 354-368.
ISSN: 0006-3002.
DOCUMENT TYPE: Article
LANGUAGE: English
ABSTRACT:
Complexes formed between **DNA** and cationic polymers are attracting increasing attention as novel synthetic vectors for delivery of genes. We are trying to improve biological properties of such complexes by oriented self-assembly of **DNA** with cationic-hydrophilic block copolymers, designed to enshroud the complex within a protective hydrophilic polymer corona. Poly(L-lysine) (pLL) grafted with range of hydrophilic polymer blocks, including poly(ethylene glycol) (pEG), dextran and poly(N-(2-hydroxypropyl)methacrylamide) (pHPMA), shows efficient binding to **DNA** and mediates particle self-assembly and inhibition of ethidium bromide/***DNA*** fluorescence. The complexes formed are discrete and typically about 100 nm diameter, viewed by **atomic force microscopy**. Surface charges are slightly shielded by the presence of the hydrophilic polymer, and complexes generally show decreased cytotoxicity compared with simple pLL/**DNA** complexes. pEG-containing complexes show increased transfection activity against cells in vitro. Complexes formed with all polymer conjugates showed greater aqueous solubility than simple pLL/**DNA** complexes, particularly at charge neutrality. These materials appear to have the ability to regulate the physicochemical and biological properties of polycation/**DNA** complexes, and should find important applications in packaging of **nucleic** acids for specific biological applications.
CONCEPT CODE: Genetics and Cytogenetics - General *03502
Microscopy Techniques - Electron Microscopy *01058
Biochemical Studies - Nucleic Acids, Purines and Pyrimidines *10062

Biochemical Studies - General *10060
INDEX TERMS: Major Concepts
Biochemistry and Molecular Biophysics
INDEX TERMS: Chemicals & Biochemicals
hydrophilic polymers; poly(L-lysine); **DNA**: self-assembly
INDEX TERMS: Methods & Equipment
atomic force microscopy: analytical method
INDEX TERMS: Miscellaneous Descriptors
gene delivery: novel vectors
REGISTRY NUMBER: 25104-18-1Q (POLY(L-LYSINE))
38000-06-5Q (POLY(L-LYSINE))

L3 ANSWER 9 OF 16 BIOSIS COPYRIGHT 2001 BIOSIS
ACCESSION NUMBER: 1998:256659 BIOSIS
DOCUMENT NUMBER: PREV199800256659
TITLE: Analysis of various sequence-specific triplexes by electron and **atomic force** microscopies.
AUTHOR(S): Cherny, Dimitry I. (1); Fourcade, Alain; Svinarchuk, Fedro; Nielsen, Peter E.; Malvy, Claude; Delain, Etienne
CORPORATE SOURCE: (1) Lab. Microscopie Cellularie Moleculaire, URA 147, CNRS, Inst. Gustave-Roussy, rue Camillie Desmoulin, F-94805 Villejuif France
SOURCE: Biophysical Journal, (Feb., 1998) Vol. 74, No. 2 PART 1, pp. 1015-1023.
ISSN: 0006-3495.
DOCUMENT TYPE: Article
LANGUAGE: English
ABSTRACT:
Sequence-specific interactions of 20-mer G,A-containing triple helix-forming oligonucleotides (TFOs) and bis-PNAs (peptide **nucleic** acids) with double-stranded **DNA** was visualized by electron (EM) and ***atomic*** **force** (AFM) microscopies. Triplexes formed by biotinylated TFOs are easily detected by both EM and AFM in which streptavidin is a marker. AFM images of the unlabeled triplex within a long plasmid ***DNA*** show a apprx0.4-nm height increment of the double helix within the target site position. TFOs conjugated to a 74-nt-long oligonucleotide forming a 33-bp-long hairpin form extremely stable triplexes with the target site that are readily imaged by both EM and AFM as protruding **DNA**. The short duplex protrudes in a perpendicular direction relative to the double helix axis, either in the plane of the support or out of it. In the latter case, the apparent height of the protrusion is apprx 1.5 nm, when that of the triplex site is increased by 0.3-0.4 nm. Triplex formation by bis-PNA, in which two decamers of PNA are connected via a flexible linker, causes deformations of the double helix at the target site, which is readily detected as kinks by both EM and AFM. Moreover, AFM shows that these kinks are often accompanied by an increase in the **DNA** apparent height of apprx 35%. This work shows the first direct visualization of sequence-specific interaction of TFOs and PNAs, with their target sequences within long plasmid DNAs, through the measurements of the apparent height of the **DNA** double helix by AFM.
CONCEPT CODE: Genetics and Cytogenetics - General *03502
Microscopy Techniques - Electron Microscopy *01098
Biochemical Methods - Nucleic Acids, Purines and Pyrimidines *10052
Biochemical Methods - Proteins, Peptides and Amino Acids *10054
Biochemical Studies - Nucleic Acids, Purines and Pyrimidines *10062
Biochemical Studies - Proteins, Peptides and Amino Acids *10064
Biophysics - Molecular Properties and Macromolecules *10506
INDEX TERMS: Major Concepts

Methods and Techniques; Molecular Genetics (Biochemistry and Molecular Biophysics)

INDEX TERMS: Chemicals & Biochemicals
bis-peptide **nucleic** acid: **DNA** interaction; double-stranded **DNA**; triple helix-forming oligonucleotide: **DNA** interaction

INDEX TERMS: Methods & Equipment
atomic force microscopy: analytical method; electron **microscopy**: analytical method

L3 ANSWER 10 OF 16 BIOSIS COPYRIGHT 2001 BIOSIS

ACCESSION NUMBER: 1998:221880 BIOSIS

DOCUMENT NUMBER: PREV199800221880

TITLE: Study of the interaction of **DNA** with cisplatin and other Pd(II) and Pt(II) complexes by **atomic force microscopy**.

AUTHOR(S): Onoa, G. Bibiana; Cervantes, Gemma; Moreno, Virtudes (1); Prieto, M. Jose

CORPORATE SOURCE: (1) Dep. Quim. Inorg., Univ. Barcelona, Diagonal 647, 08028-Barcelona Spain

SOURCE: Nucleic Acids Research, (March 15, 1998) Vol. 26, No. 6, pp. 1473-1480.
ISSN: 0305-1048.

DOCUMENT TYPE: Article

LANGUAGE: English

ABSTRACT:
Modifications in the structure of a 260 bp **DNA** (hlyM) fragment from Escherichia coli caused by interaction with Pd(II) and Pt(II) complexes were studied. Cisplatin and transplatin (cis- and trans-PtCl2(NH3)2 respectively), Pt2Cl2(Spym)4 (SPYM = 2-mercaptopyrimidine anion), Pd-famotidine and Pt-famotidine were incubated with **DNA** for 24 h at 37degreeC and then observed with an **atomic force** microscope. **Atomic** ***force*** **microscopy** (AFM) provides the opportunity for nanometer resolution in research on the interaction between **nucleic** acids and metal complexes. The complexes induced noticeable changes in **DNA** topography according to their different characteristics and structure. In the case of cisplatin a shortening in **DNA** strands was observed. Transplatin and Pt2Cl2(SPYM)4 caused shortening and compaction, whilst an aggregation of two strands was observed for the Pt-famotidine compound but not for the Pd-famotidine compound or the metal-free famotidine.

CONCEPT CODE: Biochemical Methods - Nucleic Acids, Purines and Pyrimidines *10052
Microscopy Techniques - General and Special Techniques *01052
Biochemical Methods - Minerals *10059
Biophysics - Molecular Properties and Macromolecules *10506

INDEX TERMS: Major Concepts
Biochemistry and Molecular Biophysics; Methods and Techniques

INDEX TERMS: Chemicals & Biochemicals
cisplatin: Royston, quantitative analysis; hlyM gene; palladium (II) ion: quantitative analysis; platinum (II) ion: quantitative analysis; transplatin: Royston, quantitative analysis; **DNA**: quantitative analysis

INDEX TERMS: Methods & Equipment
atomic force microscopy: **microscopy** method; polymerase chain reaction: amplification method, sequencing techniques; GeneAmp PCR system 2400: Perkin-Elmer Cetus, equipment; Nanoscope III Multimode AFM: Digital Instrumentals Inc, equipment

INDEX TERMS: Miscellaneous Descriptors
nucleic acid-metal interaction

REGISTRY NUMBER: 15663-27-1 (CISPLATIN)
16065-88-6 (PALLADIUM (II))
22542-10-5 (PLATINUM (II))
14913-33-8 (TRANSPLATIN)

L3 ANSWER 11 OF 16 BIOSIS COPYRIGHT 2001 BIOSIS
ACCESSION NUMBER: 1997:243950 BIOSIS
DOCUMENT NUMBER: PREV199799543153
TITLE: **DNA** looping by Ku and the **DNA**-dependent protein kinase.
AUTHOR(S): Cary, Robert B.; Peterson, Scott R.; Wang, Jinting; Bear, David G.; Bradbury, E. Morton; Chen, David J. (1)
CORPORATE SOURCE: (1) Life Sci. Div., Los Alamos Natl. Lab., Mail Stop M888, Los Alamos, NM 87545 USA
SOURCE: Proceedings of the National Academy of Sciences of the United States of America, (1997) Vol. 94, No. 9, pp. 4267-4272.
ISSN: 0027-8424.
DOCUMENT TYPE: Article
LANGUAGE: English
ABSTRACT:
The **DNA**-dependent protein kinase (**DNA**-PK) is required for ***DNA*** double-strand break (DSB) repair and immunoglobulin gene rearrangement and may play a role in the regulation of transcription. The ***DNA*** -PK holoenzyme is composed of three polypeptide subunits: the ***DNA*** binding Ku70/86 heterodimer and an apprxeq 460-kDa catalytic subunit (**DNA**-PKcs). **DNA**-PK has been hypothesized to assemble at **DNA** DSBs and play structural as well as signal transduction roles in DSB repair. Recent advances in **atomic** ***force*** **microscopy** (AFM) have resulted in a technology capable of producing high resolution images of native protein and proteinnucleic acid complexes without staining or metal coating. The AFM provides a rapid and direct means of probing the protein-**nucleic** acid interactions responsible for **DNA** repair and genetic regulation. Here we have employed AFM as well as electron **microscopy** to visualize Ku and ***DNA*** -PK in association with **DNA**. A significant number of ***DNA*** molecules formed loops in the presence of Ku. **DNA** looping appeared to be sequence-independent and unaffected by the presence of ***DNA*** -PKcs. Gel filtration of Ku in the absence and the presence of ***DNA*** indicates that Ku does not form nonspecific aggregates. We conclude that, when bound to **DNA**, Ku is capable of self-association. These findings suggest that Ku binding at **DNA** DSBs will result in Ku self-association and a physical tethering of the broken **DNA** strands.
CONCEPT CODE: Biochemical Studies - Nucleic Acids, Purines and Pyrimidines *10062
Biochemical Studies - Proteins, Peptides and Amino Acids *10064
Biophysics - Molecular Properties and Macromolecules *10506
Enzymes - Physiological Studies *10808
INDEX TERMS: Major Concepts
Biochemistry and Molecular Biophysics; Enzymology (Biochemistry and Molecular Biophysics)
INDEX TERMS: Chemicals & Biochemicals
PROTEIN KINASE
INDEX TERMS: Miscellaneous Descriptors
BIOCHEMISTRY AND BIOPHYSICS; **DNA**; **DNA** -DEPENDENT PROTEIN KINASE; KU70/86 HETERODIMER; LOOPING
REGISTRY NUMBER: 9026-43-1 (PROTEIN KINASE)

L3 ANSWER 12 OF 16 BIOSIS COPYRIGHT 2001 BIOSIS
ACCESSION NUMBER: 1996:150019 BIOSIS
DOCUMENT NUMBER: PREV199698722154
TITLE: **Atomic force microscopy** of

long and short double-stranded, single-stranded and triple-stranded **nucleic** acids.

AUTHOR(S): Hansma, Helen G. (1); Revenko, Irene; Kim, Kery; Laney, Daniel E.

CORPORATE SOURCE: (1) Dep. Physics, Univ. California, Santa Barbara CA 93106 USA

SOURCE: Nucleic Acids Research, (1996) Vol. 24, No. 4, pp. 713-720. ISSN: 0305-1048.

DOCUMENT TYPE: Article

LANGUAGE: English

ABSTRACT:

Atomic force microscopy (AFM, also called scanning **force microscopy**) is proving to be a useful technique for imaging **DNA**. Thus it is important to push the limits of AFM imaging in order to explore both what types of **DNA** can be reliably imaged and identified and also what substrates and methods of sample preparation are suitable. The following advances in AFM of **DNA** are presented here. (i) **DNA** molecules as short as 25 bases can be seen by AFM. The short single-stranded DNAs imaged here (25 and 50 bases long) appeared globular in the AFM, perhaps because they are all capable of intramolecular base pairing and because the DNAs were in a Mg(II) buffer, which facilitates intramolecular cross-bridging. (ii) AFM images in air of short double-stranded ***DNA*** molecules, 100-200 bp, gave lengths consistent with A-**DNA**. (iii) AFM images of poly(A) show both short bent lumpy molecules with an apparent persistence length of 40 nm and long straight molecules with an apparent persistence length of 600 nm. For comparison, the apparent persistence length for double-stranded **DNA** from vphi-X-174 under the same conditions was 80 nm. (iv) Structures believed to be triple-stranded ***DNA*** were seen in samples of poly(dA) cntdot poly(dT) and poly(dG) cntdot poly(dC). These structures were twice as high as double-stranded ***DNA*** and the same width. (v) Entire molecules of lambda **DNA**, apprx 16 mu-m long, were imaged clearly in overlapping scans. (vi) Plasmid ***DNA*** was imaged on oxidized silicon, although less clearly than on mica.

CONCEPT CODE: Microscopy Techniques - General and Special Techniques 01052
Biochemical Methods - Nucleic Acids, Purines and Pyrimidines *10052
Biochemical Studies - Nucleic Acids, Purines and Pyrimidines *10062
Biophysics - General Biophysical Techniques *10504
Biophysics - Molecular Properties and Macromolecules *10506
Physiology and Biochemistry of Bacteria *31000
Genetics of Bacteria and Viruses *31500

BIOSYSTEMATIC CODE: Bacteria - General Unspecified *05000

INDEX TERMS: Major Concepts
Biochemistry and Molecular Biophysics; Genetics; Methods and Techniques; Physiology

INDEX TERMS: Miscellaneous Descriptors
CROSS-BRIDGING; **DNA** IMAGING; INTRAMOLECULAR BASE PAIRING; LAMBDA-**DNA**; PLASMID **DNA**; SCANNING **FORCE MICROSCOPY**

ORGANISM: Super Taxa
Bacteria - General Unspecified: Eubacteria, Bacteria

ORGANISM: Organism Name
bacteria (Bacteria - General Unspecified)

ORGANISM: Organism Superterms
bacteria; eubacteria; microorganisms

L3 ANSWER 13 OF 16 BIOSIS COPYRIGHT 2001 BIOSIS

ACCESSION NUMBER: 1996:125528 BIOSIS

DOCUMENT NUMBER: PREV199698697663

TITLE: Scanning probe **microscopy** in microbiology.

AUTHOR(S): Firtel, M.,; Beveridge, T. J. (1)

CORPORATE SOURCE: (1) Department Microbiology, Faculty Medicine, University Toronto, Toronto, ON M5S 1A8 Canada

SOURCE: Micron, (1995) Vol. 26, No. 4, pp. 347-362.
ISSN: 0968-4328.

DOCUMENT TYPE: General Review

LANGUAGE: English

CONCEPT CODE: Microscopy Techniques - General and Special Techniques *01052
Biochemical Methods - Nucleic Acids, Purines and Pyrimidines *10052
Biochemical Studies - Nucleic Acids, Purines and Pyrimidines 10062
Biophysics - Molecular Properties and Macromolecules *10506
Anatomy and Histology, General and Comparative - Microscopic and Ultramicroscopic Anatomy *11108
Metabolism - Nucleic Acids, Purines and Pyrimidines *13014
Morphology and Cytology of Bacteria *30500
Physiology and Biochemistry of Bacteria *31000
Genetics of Bacteria and Viruses *31500
Microbiological Apparatus, Methods and Media *32000
Microbiological Ultrastructure *32300
Virology - Bacteriophage *33504
Virology - Animal Host Viruses *33506
Virology - Plant Host Viruses *33508

BIOSYSTEMATIC CODE: Animal Viruses - General 02600
Bacterial Viruses - General 02700
Plant Viruses - General 02800
Enterobacteriaceae 06702
Deinococcaceae 07701
Methanomicrobiaceae 09531
Halobacteriaceae *09711

INDEX TERMS: Major Concepts
Biochemistry and Molecular Biophysics; Cell Biology; Genetics; Metabolism; Methods and Techniques; Microbiology; Morphology; Physiology

INDEX TERMS: Miscellaneous Descriptors
ANALYTICAL METHOD; **ATOMIC FORCE MICROSCOPY**; BACTERIAL SURFACE LAYER; BACTERIOPHAGE SURFACE LAYER; **DNA**; MICROBIAL CELL VISCOELASTICITY; **NUCLEIC** ACID; SCANNING TUNNELLING **MICROSCOPY**; SURFACE TOPOGRAPHY; VIRAL SURFACE LAYER

ORGANISM: Super Taxa
Animal Viruses - General: Viruses; Bacterial Viruses - General: Viruses; Deinococcaceae: Eubacteria, Bacteria; Enterobacteriaceae: Eubacteria, Bacteria; Halobacteriaceae: Archaeobacteria, Bacteria; Methanomicrobiaceae: Archaeobacteria, Bacteria; Plant Viruses - General: Viruses

ORGANISM: Organism Name
animal viruses (Animal Viruses - General); bacterial viruses (Bacterial Viruses - General); Deinococcus radiodurans (Deinococcaceae); Escherichia coli (Enterobacteriaceae); Halobacterium (Halobacteriaceae); Methanospirillum hungatei (Methanomicrobiaceae); Plant Viruses (Plant Viruses - General)

ORGANISM: Organism Superterms
archaeobacteria; bacteria; eubacteria; microorganisms; viruses

L3 ANSWER 14 OF 16 BIOSIS COPYRIGHT 2001 BIOSIS

ACCESSION NUMBER: 1995:201818 BIOSIS

DOCUMENT NUMBER: PREV199598216118

TITLE: A new **DNA** nanostructure, the G-wire, imaged by

scanning probe **microscopy**.

AUTHOR(S): Marsh, Thomas C.; Vesenka, James; Henerson, Eric (1)
CORPORATE SOURCE: (1) Dep. Zool. Genet., 2112 Mol. Biol. Build., Iowa State Univ., Ames, IA 50011 USA
SOURCE: Nucleic Acids Research, (1995) Vol. 23, No. 4, pp. 696-700. ISSN: 0305-1048.
DOCUMENT TYPE: Article
LANGUAGE: English
ABSTRACT:
G-**DNA** is a polymorphic family of quadruple helical **nucleic** acid structures containing guanine tetrad motifs (G-quartets; Williamson, J.R., Raghuraman, M.K. and Cech, TR. (1989) Cell 59,871-880; Williamson, J.R. (1993) Proc. Natl. Acad Sci. USA 90, 3124-3124). Guanine rich oligonucleotides that are self-complimentary, as found in many telomeric G-strand repeat sequences, form G-**DNA** In the presence of monovalent and/or divalent metal cations. In this report we use the **atomic force** microscope (AFM) to explore the structural characteristics of long, linear polymers formed by the telomeric oligonucleotide d(GGGG TTGGGG) in the presence of specific metal cations. In the AFM these polymers, termed G-wires, appear as filaments whose height and length are determined by the metal ions present during the self-assembly process. The highly ordered, controllable self-assembly of G-wires could provide a basis for developing advanced biomaterials.
CONCEPT CODE: Microscopy Techniques - Electron Microscopy *01058
Biochemical Methods - Nucleic Acids, Purines and Pyrimidines 10052
Biochemical Studies - Nucleic Acids, Purines and Pyrimidines *10062
Biophysics - General Biophysical Techniques 10504
Biophysics - Molecular Properties and Macromolecules *10506
INDEX TERMS: Major Concepts
Biochemistry and Molecular Biophysics; Methods and Techniques
INDEX TERMS: Miscellaneous Descriptors
ANALYTICAL METHOD; **ATOMIC FORCE** MICROSCOPE; ION BIOSENSOR; OLIGONUCLEOTIDE

L3 ANSWER 15 OF 16 BIOSIS COPYRIGHT 2001 BIOSIS
ACCESSION NUMBER: 1994:327879 BIOSIS
DOCUMENT NUMBER: PREV199497340879
TITLE: **Atomic force microscopy** in basic and applied **nucleic** acid research.
AUTHOR(S): Henderson, Eric
CORPORATE SOURCE: Zool. and Genetics, Iowa State Univ., Ames, IA 50011 USA
SOURCE: Clinical Chemistry, (1994) Vol. 40, No. 4, pp. 653.
Meeting Info.: 8th San Diego Conference on Beyond DNA Probes San Diego, California, USA November 18-20, 1993
ISSN: 0009-9147.
DOCUMENT TYPE: Conference
LANGUAGE: English
CONCEPT CODE: General Biology - Symposia, Transactions and Proceedings of Conferences, Congresses, Review Annuals 00520
Microscopy Techniques - General and Special Techniques *01052
Genetics and Cytogenetics - General *03502
Biochemical Methods - Nucleic Acids, Purines and Pyrimidines *10052
Biochemical Studies - Nucleic Acids, Purines and Pyrimidines *10062
Biophysics - General Biophysical Techniques *10504
Biophysics - Molecular Properties and Macromolecules *10506
BIOSYSTEMATIC CODE: *00500
INDEX TERMS: Major Concepts

Biochemistry and Molecular Biophysics; Genetics; Methods and Techniques

INDEX TERMS: Miscellaneous Descriptors
DNA TOPOGRAPHY; MEETING ABSTRACT; VISUALIZATION METHOD

ORGANISM: Organism Name
organisms (Organisms - Unspecified)

L3 ANSWER 16 OF 16 BIOSIS COPYRIGHT 2001 BIOSIS

ACCESSION NUMBER: 1992:156807 BIOSIS

DOCUMENT NUMBER: BR42:73007

TITLE: **ATOMIC FORCE MICROSCOPY** IMAGING OF LARGE DOUBLE STRANDED **DNA** MOLECULES.

AUTHOR(S): LYUBCHENKO Y L; GALL A A; SHLYAKHTENKO L S; HARRINGTON R E; LINDSAY S M

CORPORATE SOURCE: DEP. BIOCHEMISTRY, UNIV. NEVADA RENO, RENO, NV 89557.

SOURCE: JOINT MEETING OF THE AMERICAN SOCIETY FOR BIOCHEMISTRY AND MOLECULAR BIOLOGY/BIOPHYSICAL SOCIETY, HOUSTON, TEXAS, USA, FEBRUARY 9-13, 1992. FASEB (FED AM SOC EXP BIOL) J, (1992. 6 (1), A149.
CODEN: FAJOEC. ISSN: 0892-6638.

DOCUMENT TYPE: Conference

FILE SEGMENT: BR; OLD

LANGUAGE: English

CONCEPT CODE: General Biology - Symposia, Transactions and Proceedings of Conferences, Congresses, Review Annuals 00520
Genetics and Cytogenetics - General *03502
Biochemical Studies - Nucleic Acids, Purines and Pyrimidines *10062
Biophysics - Molecular Properties and Macromolecules *10506

INDEX TERMS: Miscellaneous Descriptors
ABSTRACT GENOMIC MAPPING **NUCLEIC** ACID-PROTEIN COMPLEXES

L1 ANSWER 1 OF 18 CAPLUS COPYRIGHT 2001 ACS

ACCESSION NUMBER: 2001:171629 CAPLUS
Correction of: 1997:564938

DOCUMENT NUMBER: 134:178462
Correction of: 127:176339

TITLE: Preparation of [(pyrrolidinoalkoxy)phenyl]benzothiophenes and analogs as thrombin inhibitors

INVENTOR(S): Bastian, Jolie A.; Chirgadze, Nickolay Y.; Denney, Michael L.; Foglesong, Robert J.; Harper, Richard W.; Johnson, Mary G.; Klimkowski, Valentine J.; Kohn, Todd J.; Lin, Ho-shen; **Lynch, Michael P.**; Mccowan, Jefferson R.; Palkowitz, Alan D.; Richett, Michael E.; Sall, Daniel J.; Smith, Gerald F.; Takeuchi, Kumiko; Tinsley, Jennifer M.; Zhang, Minsheng

PATENT ASSIGNEE(S): Eli Lilly and Company, USA

SOURCE: PCT Int. Appl., 43 pp.
CODEN: PIXXD2

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LANGUAGE: English

INT. PATENT CLASSIF.:
MAIN: A61K031-34
SECONDARY: A61K031-38; A61K031-40; A61K031-42; A61K031-395; A61K031-425; A61K031-435; A61K031-495; C07D211-06; C07D241-02; C07D285-10; C07D307-78; C07D307-87; C07D307-93; C07D333-52; C07D333-56; C07D333-66; C07D333-72; C07D401-02; C07D403-14

CLASSIFICATION: 27-9 (Heterocyclic Compounds (One Hetero Atom))
Section cross-reference(s): 1

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9725033	A1	19970717	WO 1996-US17995	19961030
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, TJ, TM, TR, TT, UA, UG, US, UZ, VN, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
CA 2236007	AA	19970717	CA 1996-2236007	19961030
AU 9677255	A1	19970801	AU 1996-77255	19961030
EP 863755	A1	19980916	EP 1996-940354	19961030
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, PT, IE, SI, LT, RO				
US 6025382	A	20000215	US 1997-846647	19970430

PRIORITY APPLN. INFO.:
US 1995-7120 P 19951031
US 1996-28252 P 19961009
WO 1996-US17995 W 19961030

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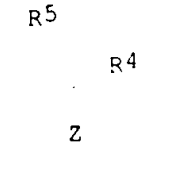

I

ABSTRACT:
Title compds. [I; R1 = 1 or 2 of H, halo, Me, OMe, CONH2, etc.; R4 = Z1Z2(CH2)j(CHR2)k(CH2)mNRaRb; R2 = OH, CH2OH, CO2Me; R5 = Z3Z4Z5(CH2)q(CHR3CHR3)rRcRd; R3 = H, alkyl, etc.; R3R3 = (CH2)3-4; Ra,Rb,Rc,Rd = H or alkyl; NRaRb,NRcRd = heterocyclyl; Z = O, S, CH:CH, CH2CH2; Z1,Z4 = 1,4-phenylene, (hetero)arylene; Z2 = bond, NH, CH2, O, S, NHCO; Z3 = O, S, CH2, CO, C:CH2; Z5 = bond, NH, CH2, O, S, etc.; j,k,r = 0 or 1; m = 0-4; q = 0-2] were prepd. Thus, benzo[b]thiophene-2-boronic acid was condensed with 4-BrC6H4OMe and the product acylated by 4-(MeO)C6H4COCl to give, after hydrolysis, I [R1 = H, R4 = C6H4(OH)-4, R5 = COC6H4(OH)-4]. The latter was etherified by 1-(2-chloroethyl)pyrrolidine to give, after redn., I [R1 = H, R4 = R, R5 = CH2R, R = 4-(2-pyrrolidinoethyl)phenyl]. Data for biol. activity of 2 prepd. I were given.

SUPPL. TERM: benzothiophene pyrrolidinoalkoxyphenyl prepn thrombin inhibitor

INDEX TERM: 9002-04-4P, Thrombin
ROLE: BAC (Biological activity or effector, except adverse); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(inhibitors; [(pyrrolidinoalkoxy)phenyl]benzothiophenes and analogs)

INDEX TERM:

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ROLE: BAC (Biological activity or effector, except adverse); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of [(pyrrolidinoalkoxy)phenyl]benzothiophenes and analogs as thrombin inhibitors)

INDEX TERM: 193964-12-4P 193964-13-5P 193964-14-6P 193967-08-7P
193968-72-8P
ROLE: BAC (Biological activity or effector, except adverse); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of [(pyrrolidinoalkoxy)phenyl]benzothiophenes and analogs as thrombin inhibitors)

INDEX TERM: 99-42-3, Methyl 4-hydroxy-3-nitrobenzoate 99-58-1,
3-Bromo-4-methoxybenzoic acid 99-76-3, Methyl
4-hydroxybenzoate 100-07-2, 4-Anisoyl chloride 100-35-6,
2-Diethylaminoethyl chloride 104-92-7, 4-Bromoanisole
106-40-1, 4-Bromoaniline 106-53-6, 4-Bromobenzenethiol
107-19-7, Propargyl alcohol 108-01-0, 2-
Dimethylaminoethanol 109-89-7, Diethylamine, reactions
110-91-8, Morpholine, reactions 122-04-3, 4-Nitrobenzoyl
chloride 123-75-1, Pyrrolidine, reactions 150-76-5,
4-Methoxyphenol 271-89-6, Benzofuran 285-67-6,
Cyclopentene oxide 286-20-4, Cyclohexene oxide 288-32-4,
Imidazole, reactions 351-54-2, 3-Fluoro-p-anisaldehyde
403-43-0, 4-Fluorobenzoyl chloride 533-68-6, Ethyl
2-bromobutyrate 589-15-1, 4-Bromobenzyl bromide
619-58-9, 4-Iodobenzoic acid 624-28-2, 2,5-Dibromopyridine
696-62-8, 4-Iodoanisole 758-16-7, N,N-
Dimethylthioformamide 816-40-0, 1-Bromo-2-butanone
876-08-4, 4-Chloromethylbenzoyl chloride 1007-16-5,
3-Bromo-4-fluorobenzoic acid 1081-73-8,
1-[2-(4-Bromophenoxy)ethyl]pyrrolidine 1200-07-3,
4-Bromocinnamic acid 1461-25-2, Tetrabutyltin 2033-76-3,
1-(2-Bromoethoxy)-4-chlorobenzene 2176-98-9,
Tetrapropyltin 2362-12-1, 4-Bromo-2-methylphenol
2426-87-1, 4-Benzyloxy-3-methoxybenzaldehyde 2555-88-6,
1-Pyrrolidineethanol 3535-37-3, 3,4-Dimethoxybenzoyl
chloride 3556-83-0, Methyl 3-methoxy-4-methylbenzoate
3647-69-6, 4-(2-Chloroethyl)morpholine hydrochloride
3943-74-6, Methyl vanillate 4397-53-9,
4-Benzyloxybenzaldehyde 4465-44-5, L-Serine,
N-triphenylmethyl-, methyl ester 4654-39-1,
4-Bromobenzeneethanol 5326-23-8, 6-Chloronicotinic acid
5335-87-5, Bis(4-methoxyphenyl) disulfide 6091-44-7,
Piperidine hydrochloride 6232-88-8, 4-Bromomethylbenzoic
acid 7217-59-6, 2-Methoxybenzenethiol 7250-67-1,

1-(2-Chloroethyl)pyrrolidine hydrochloride 7342-82-7, 3-Bromobenzo[b]thiophene 7368-78-7, 4-Bromo-2-methoxyphenol 10068-07-2, Methyl 3-hydroxyisoxazole-5-carboxylate 14315-14-1, 5-Methylbenzo[b]thiophene 14909-79-6, trans-2-(4-Morpholinyl)cyclohexanol 14909-81-0, trans-2-(1-Pyrrolidinyl)cyclohexanol 15570-12-4, 3-Methoxybenzenethiol 19748-66-4, 1-Pyrrolidinepropanol 23356-96-9, (S)-Prolinol 40663-68-1, 4-Allyloxybenzaldehyde 41110-33-2, Methyl 5-methylpyridazine-2-carboxylate 52062-92-7, 4-(2-Bromoethyl)benzoic acid 56525-63-4, Methyl 3-chloro-4-methylbenzoate 60441-79-4, Methyl 3,5-dimethoxy-4-methylbenzoate 60876-70-2, 4-tert-Butoxybromobenzene 63126-47-6, (S)-2-Methoxymethylpyrrolidine 63675-90-1, 4-[2-(1-Pyrrolidinyl)ethoxy]benzoic acid hydrochloride 67515-55-3, 4-Fluoro-3-trifluoromethylbenzoic acid 68832-13-3 73200-24-5, 4-Oxo-4-(1-pyrrolidinyl)butyric acid 76903-88-3, 3,4-Difluorobenzoyl chloride 84449-74-1, 4-[2-Hexahydro-1H-azepin-1-yl)ethoxy]benzoic acid 98437-23-1, Benzo[b]thiophene-2-boronic acid 104901-43-1, Methyl 3-bromo-4-methylbenzoate 111359-29-6, 2-Dimethylamino-6-methoxybenzo[b]thiophene 115314-17-5 169191-79-1 193967-03-2 193967-04-3, Triisopropylsilyl methanesulfonate 193967-05-4
ROLE: RCT (Reactant)
(prepn. of [(pyrrolidinoalkoxy)phenyl]benzothiophenes and analogs as thrombin inhibitors)

INDEX TERM: 2401-47-0P, N,N-Dimethyl-2-(4-chlorophenoxy)ethanamine 2564-02-5P, N-(4-Bromophenyl)chloroacetamide 3781-90-6P, 4-Methoxybenzo[b]thiophene 4897-55-6P, 1-Bromo-4-[(1-pyrrolidinyl)methyl]benzene 4923-87-9P, 5-Bromobenzo[b]thiophene 7432-60-2P, trans-2-Diethylaminocyclohexanol 7581-94-4P, trans-2-(1-Piperidinyl)cyclohexanol 13734-70-8P 15910-74-4P, trans-2-Dimethylaminocyclohexanol 19234-04-9P, 2-(4-Methoxyphenyl)benzofuran 20532-30-3P, 5-Methoxybenzo[b]thiophene 26563-22-4P, 3-Bromo-2-(4-methoxyphenyl)benzo[b]thiophene 27884-09-9P, 2-(4-Methoxyphenyl)benzo[b]thiophene 42302-16-9P, 2-(1-Pyrrolidinyl)ethanethiol 51217-01-7P 55307-73-8P, 1-(1-Pyrrolidinyl)-2-butanol 63675-96-7P 63676-04-0P 63676-05-1P 63676-06-2P 63676-08-4P 63676-12-0P 63712-58-3P 63712-60-7P 67515-56-4P, 4-Fluoro-3-trifluoromethylbenzoyl chloride 79664-44-7P, Methyl 4-bromomethyl-3-methoxybenzoate 74733-30-5P, Methyl 4-bromomethyl-3-chlorobenzoate 78946-25-5P, Methyl 3-Bromo-4-bromomethylbenzoate 88791-08-6P, 7-Methoxybenzo[b]thiophene 89473-71-2P, N-(4-Bromophenyl)-2-(1-pyrrolidinyl)acetamide 90560-10-4P, 6-Methoxybenzo[b]thiophene 93264-47-2P, 4-(1-Pyrrolidinyl)-1-butanol 96803-64-4P 97073-14-8P, 1-(1-Pyrrolidinyl)-2-butanone 129500-93-2P, trans-2-(1-Imidazolyl)cyclohexanol 132833-51-3P 136099-65-5P, Boronic acid, (5-methylbenzo[b]thien-2-yl)- 140911-50-8P 160598-45-8P 170847-71-9P 170847-74-2P 174264-46-1P 180916-06-7P, 5-Bromo-2-[2-(1-pyrrolidinyl)ethoxy]pyridine 182133-35-3P, 6-Methoxybenzo[b]thiophene-2-boronic acid 185415-35-4P 185415-46-7P, 2-Dimethylamino-5-fluoro-6-Methoxybenzo[b]thiophene 185416-86-8P 189940-52-1P 193960-93-9P 193960-96-2P 193961-08-9P 193961-10-3P 193964-15-7P 193964-16-8P 193964-17-9P 193964-18-0P 193964-19-1P 193964-20-4P, Methyl 4-[3-(1-

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3-(4-Methoxyphenoxy)benzo[b]thiophene 193964-35-1P
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193966-15-3P
ROLE: RCT (Reactant); SPN (Synthetic preparation); PREP
(Preparation)
(prepn. of [(pyrrolidinoalkoxy)phenyl]benzothiophenes and
analogs as thrombin inhibitors)

INDEX TERM:

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193966-50-6P 193966-52-8P 193966-54-0P 193966-55-1P
193966-56-2P, 2-(4-tert-Butoxyphenyl)-6-

methoxybenzo[b]thiophene 193966-57-3P 193966-58-4P, 7-Fluoro-2-(4-hydroxyphenyl)-6-methoxybenzo[b]thiophene 193966-59-5P 193966-60-8P 193966-61-9P 193966-62-0P 193966-63-1P 193966-64-2P 193966-65-3P, Methyl 3-bromo-4-dimethylaminomethylbenzoate 193966-66-4P 193966-67-5P 193966-68-6P 193966-69-7P 193966-70-0P, Methyl 5-bromomethylpyrazine-2-carboxylate 193966-71-1P 193966-72-2P 193966-73-3P 193966-74-4P 193966-75-5P 193966-76-6P 193966-77-7P, 1-Bromo-4-triisopropylsilyloxybenzene 193966-78-8P 193966-79-9P 193966-80-2P 193966-81-3P 193966-82-4P 193966-83-5P 193966-84-6P 193967-06-5P 193968-71-7P 193968-73-9P 193968-74-0P
ROLE: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation)
(prepn. of [(pyrrolidinoalkoxy)phenyl]benzothiophenes and analogs as thrombin inhibitors)

INDEX TERM: 193966-85-7P 193966-86-8P 193966-87-9P 193966-88-0P 193966-89-1P 193966-90-4P 193966-91-5P 193966-92-6P 193966-93-7P 193966-94-8P 193966-95-9P 193966-96-0P 193966-97-1P 193966-98-2P 193966-99-3P 193967-00-9P 193967-01-0P 193967-02-1P
ROLE: SPN (Synthetic preparation); PREP (Preparation)
(prepn. of [(pyrrolidinoalkoxy)phenyl]benzothiophenes and analogs as thrombin inhibitors)

L1 ANSWER 2 OF 18 CAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 1999:625538 CAPLUS
DOCUMENT NUMBER: 131:351185
TITLE: Solid phase chemistry approach to the SAR development of a novel class of active site-directed thrombin inhibitors
AUTHOR(S): Johnson, Mary George; Bronson, Duane D.; Gillespie, Jan E.; Gifford-Moore, Donetta S.; Kalter, Kyomi; **Lynch, Michael P.**; McCowan, Jefferson R.; Redick, Catherine C.; Sall, Daniel J.; Smith, Gerald F.; Foglesong, Robert J.
CORPORATE SOURCE: Sphinx Pharmaceuticals, A Division of Eli Lilly and Company, Durham, NC, 27707, USA
SOURCE: Tetrahedron (1999), 55(39), 11641-11652
CODEN: TETRAB; ISSN: 0040-4020
PUBLISHER: Elsevier Science Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English
CLASSIFICATION: 27-9 (Heterocyclic Compounds (One Hetero Atom))
Section cross-reference(s): 1

ABSTRACT:
A solid phase chem. approach utilizing Mitsunobu chem., amine functionalization, and parallel purifn. was used to produce a diverse library of benzothiophene analogs. These analogs were used to advance the SAR of this class of mols. and give new directions for future studies.

SUPPL. TERM: benzothiophene solid phase prepn thrombin inhibitor
INDEX TERM: 9002-04-4, Thrombin
ROLE: BPR (Biological process); BIOL (Biological study); PROC (Process)
(inhibitors; solid phase prepn. of benzothiophenes as active site-directed thrombin inhibitors)

INDEX TERM: 250651-28-6P 250651-29-7P 250651-30-0P 250651-32-2P 250651-33-3P 250651-34-4P 250651-35-5P 250651-36-6P 250651-37-7P 250651-38-8P 250651-39-9P 250651-40-2P 250651-42-4P
ROLE: BAC (Biological activity or effector, except adverse); SPN (Synthetic preparation); BIOL (Biological study); PREP

(Preparation)
(solid phase prepn. of benzothiophenes as active site-directed thrombin inhibitors)

INDEX TERM: 250651-25-3 250651-27-5
ROLE: RCT (Reactant)
(solid phase prepn. of benzothiophenes as active site-directed thrombin inhibitors)

INDEX TERM: 166975-45-7DP, polymer bound
ROLE: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation)
(solid phase prepn. of benzothiophenes as active site-directed thrombin inhibitors)

INDEX TERM: 250651-26-4P
ROLE: SPN (Synthetic preparation); PREP (Preparation)
(solid phase prepn. of benzothiophenes as active site-directed thrombin inhibitors)

REFERENCE COUNT: 24

REFERENCE(S):

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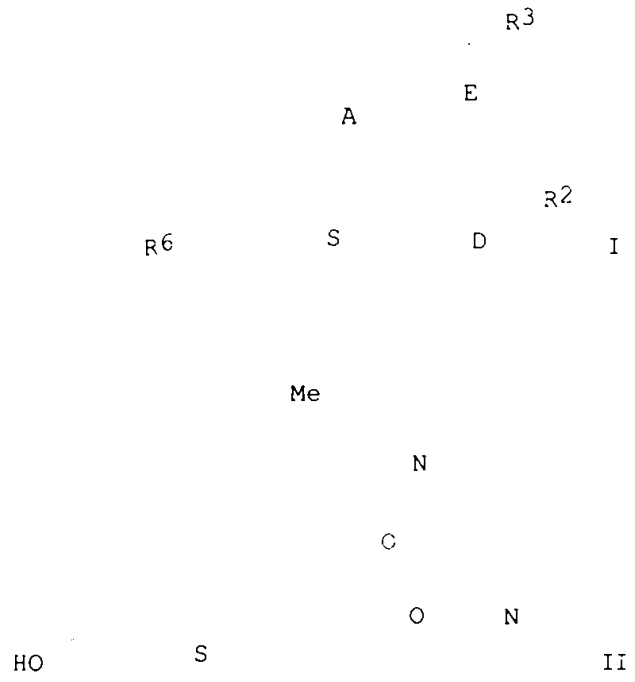
L1 ANSWER 3 OF 18 CAPLUS COPYRIGHT 2001 ACS

ACCESSION NUMBER: 1998:721694 CAPLUS
DOCUMENT NUMBER: 129:343408
TITLE: Preparation of 3-benzyl(or benzoyl)-2-phenylbenzo[b]thiophenes as antithrombotic agents
INVENTOR(S): Bach, Nicholas J.; Bastian, Jolie A.; Chirgadze, Nickolay Y.; Denney, Michael L.; Foglesong, Robert J.; Harper, Richard W.; Johnson, Mary G.; Lin, Ho-shen; **Lynch, Michael P.**; McCowan, Jefferson R.; Palkowitz, David A.; Sall, Daniel J.; Smith, Gerald F.; Takeuchi, Kumiko; Zhang, Minsheng
PATENT ASSIGNEE(S): Eli Lilly and Co., USA
SOURCE: PCT Int. Appl., 138 pp.
CODEN: PIXXD2

DOCUMENT TYPE: Patent
LANGUAGE: English
INT. PATENT CLASSIF.:
MAIN: C07D409-14
CLASSIFICATION: 27-9 (Heterocyclic Compounds (One Hetero Atom))
Section cross-reference(s): 1, 63
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9849161	A1	19981105	WO 1998-US8830	19980430
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, GM, GW, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
AU 9872740	A1	19981124	AU 1998-72740	19980430
EP 980367	A1	20000223	EP 1998-920094	19980430
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, NL, SE, PT, IE, FI				

PRIORITY APPLN. INFO.: US 1997-44297 19970430
WO 1998-US8830 19980430
OTHER SOURCE(S): MARPAT 129:343408
GRAPHIC IMAGE:



ABSTRACT:
The title compds. [I; A = C(O), CH2; D = CH, C(OH), CMe, C(OMe), N; E = CH, CMe, C(OMe), C(halo); R2 = X2(CH2)mNRaRb (wherein X2 = a direct bond, CH2, O, S; m = 1-5; provided that when m = 1, then X2 = a direct bond; Ra, Rb = H, C1-3 alkyl; NRaRb = pyrrolidino, piperidino, morpholino); R3 = ON(Rg)2, SRh, CORi,

etc. (wherein R9 = Me, Et; Rh = 2-thiazolyl; Ri = MeO); R6 = H, OH, MeO] and their pharmaceutically acceptable salts, useful as thrombin inhibitors, were prepd. and formulated. Thus, e.g., a multi-step synthesis of the title compd. II.oxalate, starting with 4-benzyloxybenzaldehyde, was described. Compds. I are effective at 0.01-1000 mg/kg/day.

SUPPL. TERM: antithrombotic agent benzylphenylbenzothiophene benzoylphenylbenzothiophene prepn formulation; thrombin inhibitor benzylphenylbenzothiophene benzoylphenylbenzothiophene prepn formulation; benzothiophene prepn formulation antithrombotic

INDEX TERM: Antithrombotics
Thrombin inhibitors
(prepn. of 3-benzyl(or benzoyl)-2-phenylbenzo[b]thiophenes as antithrombotic agents)

INDEX TERM: 215605-16-6P 215605-40-6P
ROLE: BAC (Biological activity or effector, except adverse ; RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of 3-benzyl(or benzoyl)-2-phenylbenzo[b]thiophenes as antithrombotic agents)

INDEX TERM: 215604-83-4P 215604-84-5P 215604-86-7P 215604-88-9P
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215604-93-6P 215604-94-7P 215604-95-8P 215604-96-9P
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215605-12-2P 215605-13-3P 215605-14-4P 215605-15-5P
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215605-26-8P 215605-27-9P 215605-28-0P 215605-29-1P
215605-30-4P 215605-31-5P 215605-32-6P 215605-33-7P
215605-34-8P 215605-35-9P 215605-37-1P 215605-39-3P
215605-41-7P 215605-43-9P 215605-44-0P
ROLE: BAC (Biological activity or effector, except adverse ; SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of 3-benzyl(or benzoyl)-2-phenylbenzo[b]thiophenes as antithrombotic agents)

INDEX TERM: 85-41-6, Phthalimide 105-36-2, Ethyl bromoacetate 120-92-3, Cyclopentanone 121-34-6, Vanillic acid 286-20-4, 7-Oxabicyclo[4.1.0]heptane 288-94-8, 1H-Tetrazole 403-16-7, 3-Chloro-4-fluorobenzoic acid 403-43-0, p-Fluorobenzoyl chloride 497-25-6, 2-Oxazolidone 766-00-7, 2-Cyclopentylethanol 1081-73-8 2417-72-3, Methyl 4-bromomethylbenzoate 2749-11-3, (S)-2-Amino-1-propanol 2969-81-5, Ethyl 4-bromobutyrate 3195-95-7, 2-Pyrrolidone sodium salt 3445-11-2, 1-(2-Hydroxyethyl)-2-pyrrolidinone 3556-83-0, Methyl 3-methoxy-4-methylbenzoate 3699-54-5, 1-(2-Hydroxyethyl)-2-imidazolidinone 3710-84-7, N,N-Diethylhydroxylamine 4397-53-9, 4-Benzyloxybenzaldehyde 5454-83-1, Methyl 5-bromovalerate 5685-05-2, 2-Mercaptothiazole 7250-67-1 7368-78-7, 4-Bromoguaiacol 7697-28-1, 4-Bromo-3-methylbenzoic acid 13865-19-5, Methyl 3-formylpropionate 18190-44-8, N-(2-Hydroxyethyl)succinimide 25542-62-5, Ethyl 6-bromohexanoate 34743-89-9 38328-23-1 58029-83-7 63675-96-7 77470-53-2, 4-Chloromethyl-2-methylthiazole hydrochloride 90560-10-4, 6-Methoxybenzo[b]thiophene 104901-43-1, Methyl 3-bromo-4-methylbenzoate 193964-19-1 193966-49-3 193966-83-5
ROLE: RCT (Reactant)

(prepn. of 3-benzyl(or benzoyl)-2-phenylbenzo[b]thiophenes as antithrombotic agents)

INDEX TERM: 63675-97-8P 63675-98-9P 63676-01-7P 70264-94-3P
78946-25-5P 87767-87-1P 106727-83-7P 133305-43-8P
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215607-08-2P
ROLE: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation)
(prepn. of 3-benzyl(or benzoyl)-2-phenylbenzo[b]thiophenes as antithrombotic agents)

L1 ANSWER 4 OF 18 CAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 1998:719268 CAPLUS
DOCUMENT NUMBER: 129:343406
TITLE: Preparation of benzothiophenes as antithrombotic agents
INVENTOR(S): Chirgadze, Nickolay Y.; Denney, Michael L.; Fisher, Matthew J.; Foglesong, Robert J.; Harper, Richard W.; Johnson, Mary G.; Lin, Ho-shen; **Lynch, Michael P.**; McCowan, Jefferson R.; Miller, Shawn C.; Palkowitz, Alan D.; Richett, Michael E.; Sall, Daniel Jon; Smith, Gerald Floyd; Takeuchi, Kumiko; Zhang, Minsheng
PATENT ASSIGNEE(S): Eli Lilly and Co., USA
SOURCE: PCT Int. Appl., 171 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
INT. PATENT CLASSIF.:
MAIN: A61K031-445
SECONDARY: A61K031-38
CLASSIFICATION: 27-9 (Heterocyclic Compounds (One Hetero Atom))
Section cross-reference(s): 1, 63
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9848804	A1	19981105	WO 1998-US8717	19980430
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, GM, GW, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
AU 9874700	A1	19981124	AU 1998-74700	19980430
EP 1027051	A1	20000816	EP 1998-922073	19980430

R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, PT, IE
PRIORITY APPLN. INFO.: US 1997-45188 P 19970430
WO 1998-US8717 W 19980430
OTHER SOURCE(S): MARPAT 129:343406
GRAPHIC IMAGE:

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

ABSTRACT:
The title compds. [I; A = C(O), CH2; D = CH, CMe, C(OMe), N; E = CH, CMe, C(OMe), C(halo), N; R2 = NRaCO(CH2)mRb, OCH2Rb, NHCORg, etc. (wherein m = 0-1; Ra = H, Me; Rb = II, III (G = O, S, NH, CH2, CH2CH2; Rc = H, Me; L = NH, NMe, CH2; Rg = 5-membered heteroarom. having 2 heteroatoms selected from O, S and N in which the carbonyl group is bonded to a ring carbon situated between a ring heteroatom and another ring carbon, etc.)); R3 = X3(CH2)sNRsRt (X3 = a direct bond, CH2, O; s = 1-2; provided that when s = 1, then X3 = a direct bond; and Rs and Rt = H, C1-3 alkyl or NRsRt = pyrrolidino, piperidino, morpholino); R6 = H, OH, MeO] and their pharmaceutically acceptable salts, useful as thrombin inhibitors, were prepd. and formulated. Thus, a multi-step synthesis of the title compd. (R)-IV oxalate, starting with 6-methoxybenzo[b]thiophene, is described. Compds. I are effective at 0.01-1000 mg/kg/day.

SUPPL. TERM: benzothiophene prepn formulation antithrombotic; thrombin inhibitor benzothiophene prepn formulation

INDEX TERM: Antithrombotics
Thrombin inhibitors
(prepn. of benzothiophenes as antithrombotic agents)

INDEX TERM: 215387-83-0P
ROLE: BAC (Biological activity or effector, except adverse); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of benzothiophenes as antithrombotic agents)

INDEX TERM:

215386-99-5P	215387-00-1P	215387-02-3P	215387-03-4P
215387-04-5P	215387-05-6P	215387-08-9P	215387-09-0P
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ROLE: BAC (Biological activity or effector, except adverse); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of benzothiophenes as antithrombotic agents)

INDEX TERM: 55-22-1, Isonicotinic acid, reactions 65-85-0, Benzoic

acid, reactions 79-44-7, Dimethylcarbamoyl chloride
96-30-0, 2-Chloro-N-methylacetamide 98-09-9,
Benzenesulfonyl chloride 98-78-2 98-79-3,
2-Pyrrolidinone-5-carboxylic acid 104-92-7, 4-Bromoanisole
106-41-2, 4-Bromophenol 122-04-3, 4-Nitrobenzoyl chloride
123-75-1, Pyrrolidine, reactions 403-43-0, 4-Fluorobenzoyl
chloride 534-03-2 586-78-7, 1-Bromo-4-nitrobenzene
611-73-4, Benzoylformic acid 623-00-7, 4-Bromobenzonitrile
628-20-6, 4-Chlorobutyronitrile 766-00-7,
2-Cyclopentylethanol 1072-84-0, 4-Imidazolecarboxylic acid
1192-63-8, 1-Pyrrolidinecarbonyl chloride 1621-91-6,
3-Pyrazolecarboxylic acid 2362-12-1 2675-89-0,
2-Chloro-N,N-dimethylacetamide 2955-88-6,
1-(2-Hydroxyethyl)pyrrolidine 3209-71-0,
3-Isoxazolecarboxylic acid 3445-11-2, 1-(2-Hydroxyethyl)-2-
pyrrolidinone 3556-83-0, Methyl 3-methoxy-4-methylbenzoate
3699-54-5, 1-(2-Hydroxyethyl)-2-imidazolidinone 3770-22-7,
6-Oxo-2-piperidinecarboxylic acid 3943-[illegible]-6, Methyl
4-hydroxy-3-methoxybenzoate 4042-36-8, D-Pyroglutamic acid
4397-53-9, 4-Benzyloxybenzaldehyde 5089-33-8,
4-Bromo-N,N-bis(trimethylsilyl)aniline 5332-06-9,
4-Bromobutyronitrile 7250-67-1, 1-(2-
Chloroethyl)pyrrolidine hydrochloride 7268-43-1
15159-40-7, 4-Morpholinecarbonyl chloride 17342-08-4,
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32741-98-3 34743-88-9, 2-(4-Bromophenoxy)ethanol
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73918-56-6 76453-38-8 80522-42-5, Triisopropylsilyl
trifluoromethanesulfonate 84449-68-3 90560-10-4,
6-Methoxybenzo[b]thiophene 97899-36-0 98437-23-1,
Benzo[b]thiophene-2-boronic acid 104901-43-1, Methyl
3-bromo-4-methylbenzoate 175460-94-3, 6-Methoxy-2-(4-
hydroxyphenyl)benzo[b]thiophene 193964-97-5 193964-98-6
215386-65-5 215386-71-3 215386-76-8 215388-71-9
ROLE: RCT (Reactant)
(prepn. of benzothiophenes as antithrombotic agents)

INDEX TERM:
15546-08-4P 27884-09-9P 63676-06-2P 63676-12-0P
65540-08-1P 70264-94-7P 78946-25-5P 106391-86-0P
182133-35-3P 193964-66-8P 193964-75-9P 193964-77-1P
193965-54-7P 193965-55-8P 193965-93-4P 193965-94-5P
193966-02-8P 193966-03-9P 193966-04-0P 193966-06-2P
193966-34-6P 193966-35-7P 193966-77-7P,
1-Bromo-4-(triisopropylsilyloxy)benzene 193966-78-8P
193966-79-9P 193966-80-2P 215378-95-3P 215378-96-4P
215379-00-3P 215379-09-2P 215379-15-0P 215379-57-0P
215380-08-8P 215380-13-5P 215382-00-6P 215382-22-2P
215382-32-4P 215382-37-9P 215382-64-2P 215382-97-1P
215383-02-1P 215383-70-3P 215383-72-5P 215383-91-8P
215383-94-1P 215383-99-6P 215384-02-4P 215384-17-1P
215384-28-4P 215384-46-6P 215384-57-9P 215384-62-6P
215384-91-1P 215387-32-9P 215388-21-9P 215388-22-0P
215388-23-1P 215388-24-2P 215388-26-4P 215388-27-5P
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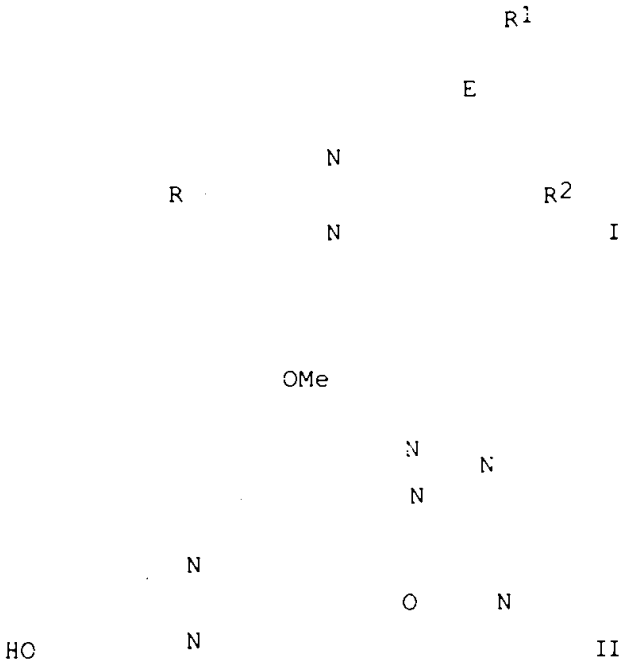
215388-55-9P 215388-57-1P 215388-58-2P 215388-59-3P
215388-61-7P 215388-62-8P 215388-63-9P 215388-64-0P

215388-66-2P 215388-67-3P 215388-68-4P 215388-69-5P
215388-70-8P
ROLE: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation)
(prepn. of benzothiophenes as antithrombotic agents)

L1 ANSWER 5 OF 18 CAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 1998:719264 CAPLUS
DOCUMENT NUMBER: 130:3845
TITLE: Preparation of 1-benzyl-2-phenylbenzimidazoles as antithrombotic agents
INVENTOR(S): Bastian, Jolie A.; Chirgadze, Nickolay Y.; Denney, Michael L.; Fisher, Matthew J.; Foglesong, Robert J.; Harper, Richard W.; Johnson, Mary G.; Klimkowski, Valentine J.; Lin, Ho-shen; **Lynch, Michael P.**; McCowan, Jefferson R.; Miller, Shawn C.; Mullaney, Jeffrey T.; Richett, Michael E.; Sall, Daniel J.; Smith, Gerald F.; Takeuchi, Kumiko; Tinsley, Jennifer M.; Wiley, Michael R.; Zhang, Minsheng
PATENT ASSIGNEE(S): Eli Lilly and Co., USA
SOURCE: PCT Int. Appl., 75 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
INT. PATENT CLASSIF.:
MAIN: A61K031-415
SECONDARY: A61K031-41
CLASSIFICATION: 28-9 (Heterocyclic Compounds (More Than One Hetero Atom))
Section cross-reference(s): 1, 63
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9848800	A1	19981105	WO 1998-US8755	19980430
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, GM, GW, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
AU 9872707	A1	19981124	AU 1998-72707	19980430
EP 1019047	A1	20000719	EP 1998-920057	19980430
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, NL, SE, PT, IE, FI				

PRIORITY APPLN. INFO.: US 1997-45335 P 19970501
WO 1998-US8755 W 19980430
OTHER SOURCE(S): MARPAT 130:3845
GRAPHIC IMAGE:



ABSTRACT:
The title compds. [I; E = CH, CMe, C(OMe), C(halo); R denotes 0-2 substituents selected from halo, Me, Et, etc.; R1 = 5-tetrazolylmethyl, 2-carboxypyrrolidin-1-ylmethyl, etc. R2 = 2-(1-pyrazolyl)ethoxy, 2-(1-pyrrolidinyl)ethoxy, etc.] and their pharmaceutically acceptable salts, useful as thrombin inhibitors, were prepd. and formulated. Thus, a multi-step synthesis of the title compd. II as its dioxalate salt, starting with 4-amino-3-nitrophenol, was described. Preferred compds. I reduce the net clot wt. to approx. 25-30% of control, or even lower, at an i.v. dose of 33.176 .mu.mol/kg/h.

SUPPL. TERM: benzylphenylbenzimidazole prepn formulation antithrombotic; thrombin inhibitor benzylphenylbenzimidazole prepn formulation

INDEX TERM: Antithrombotics
Thrombin inhibitors
(prepn. of 1-benzyl-2-phenylbenzimidazoles as antithrombotic agents)

INDEX TERM: 215656-86-3P 215656-88-5P 215656-90-9P 215656-91-0P 215656-92-1P 215656-93-2P 215656-94-3P 215656-96-5P 215656-97-6P 215656-98-7P
ROLE: BAC (Biological activity or effector, except adverse); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of 1-benzyl-2-phenylbenzimidazoles as antithrombotic agents)

INDEX TERM: 50-85-1, 4-Methylsalicylic acid 98-88-4, Benzoyl chloride 99-96-7, reactions 100-46-9, Benzylamine, reactions 288-13-1, Pyrazole 610-81-1, 4-Amino-3-nitrophenol 616-45-5, 2-Pyrrolidinone 1493-27-2, 2-Fluoronitrobenzene 5587-42-8, Imidazole sodium salt 7250-67-1 40958-42-1, Pyrazole sodium salt 41253-21-8, 1,2,4-Triazole sodium salt 63675-91-2 69731-93-7 193964-75-9
ROLE: RCT (Reactant)
(prepn. of 1-benzyl-2-phenylbenzimidazoles as antithrombotic agents)

INDEX TERM: 99-76-3P 56850-91-0P 63675-89-8P 63675-90-1P

74733-27-0P 81245-24-1P 122893-33-8P 193964-76-0P
215656-53-4P 215656-54-5P 215656-55-6P 215656-60-3P
215656-61-4P 215656-64-7P 215656-65-8P 215656-66-9P
215656-70-5P 215656-99-8P 215657-00-4P 215657-01-5P
215657-02-6P 215657-03-7P 215657-04-8P 215657-05-9P
215657-06-0P 215657-07-1P 215657-08-2P [illegible]
ROLE: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation)
(prepn. of 1-benzyl-2-phenylbenzimidazoles as antithrombotic agents)

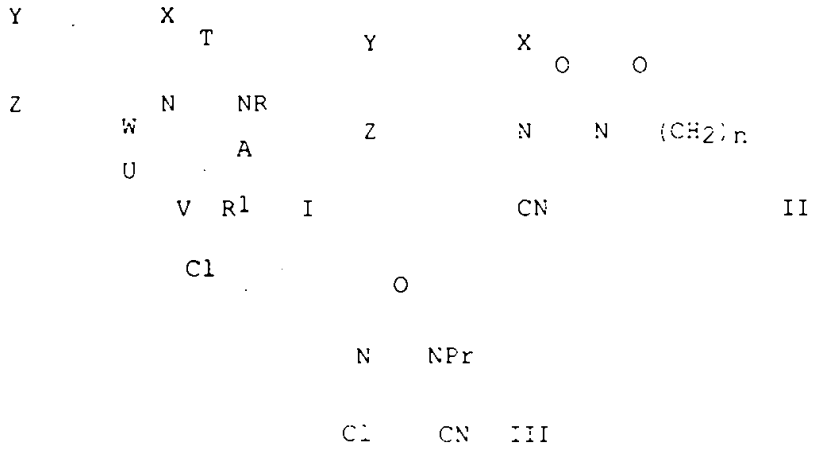
REFERENCE COUNT: 2
REFERENCE(S): (1) Lunn; US 5552426 A 1996 CAPLUS
(2) Narr; US 5541229 A 1996 CAPLUS

L1 ANSWER 6 OF 18 CAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 1993:124535 CAPLUS
DOCUMENT NUMBER: 118:124535
TITLE: Preparation of phenylimidazolone herbicides and intermediates
INVENTOR(S): Crouse, Gary D.; **Lynch, Michael P.**; Webster, Jeffery D.; Wright, John P.
PATENT ASSIGNEE(S): USA
SOURCE: U.S., 36 pp.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
INT. PATENT CLASSIF.:
MAIN: C07D211-40
SECONDARY: C07D267-12
US PATENT CLASSIF.: 540451000
CLASSIFICATION: 28-9 (Heterocyclic Compounds (More Than One Hetero Atom))
Section cross-reference(s): 5
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 5153316	A	19921006	US 1991-710223	19910604
WO 9221662	A1	19921210	WO 1992-US4716	19920604
W: AT, AU, BB, BG, BR, CA, CH, DE, DK, ES, FI, GB, HU, JP, KP, KR, LK, LU, MG, MW, NL, NO, PL, RO, RU, SD, SE, US				
RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, DE, DK, ES, FR, GA, GB, GN, GR, IT, LU, MC, ML, MR, NL, SE, SN, TD, TG				
AU 9221623	A1	19930108	AU 1992-21623	19920604

PRIORITY APPLN. INFO.: US 1991-710223 19910604
WO 1992-US4716 19920604

OTHER SOURCE(S): MARPAT 118:124535
GRAPHIC IMAGE:



ABSTRACT:
Herbicides [I; A = bond, C:T; R = H, alkyl, haloalkyl, cyanoalkyl, Ph; R1 = H, halo, (halo)alkyl, cyano; when A = bond, RR1 = atoms to form an (unsatd.) (substituted) 3-7 membered carbocyclic ring; T = O, S; U = H; V = OH; or UV = bond; W = halo, cyano; when W = halo, then R1 = cyano; X = H, halo; Y = H, halo, cyano, alkyl, CH3, OCF3; Z = H, halo, OH, alkyl, aryloxy, alkyl, (acyl)amino, NO2, alkoxy; YZ = atoms to form a (substituted) (unsatd.) 3-7 membered carbocyclic ring], and intermediates II (n = 1-4, other variables as above), were prepd. Thus, 1-(4-chlorophenyl)-4-formyl-5-chloro-3-propyl-1,3-dihydro-2H-imidazol-2-one was stirred with NH2OH.HCl in EtOH/H2O and the product was stirred with Cl3CCOCl/Et3N in CH2Cl2 to give title compd. III. III at 0.5 lb/acre preemergent gave complete control of; jimsonweed, foxtail millet, lambsquarter, etc.

SUPPL. TERM: phenylimidazolone prepn herbicide; imidazolone phenyl herbicide

INDEX TERM: Herbicides
(phenylimidazolones)

INDEX TERM:

145861-66-1P	145861-67-2P	145861-68-3P	145861-69-4P
145861-70-7P	145861-71-8P	145861-72-9P	145861-73-0P
145861-74-1P	145861-75-2P	145861-76-3P	145861-77-4P
145861-78-5P	145861-79-6P	145861-80-9P	145861-81-0P
145861-82-1P	145861-83-2P	145861-84-3P	145861-85-4P
145861-86-5P	145861-87-6P	145861-88-7P	145861-89-8P
145861-90-1P	145861-91-2P	145861-92-3P	145861-93-4P
145861-94-5P	145861-95-6P	145861-96-7P	145861-97-8P
145861-98-9P	145861-99-0P	145862-00-6P	145862-01-7P
145862-02-8P	145862-03-9P	145862-04-0P	145862-05-1P
145862-06-2P	145862-07-3P	145862-08-4P	145862-09-5P
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145862-18-6P	145862-19-7P	145862-20-0P	145862-21-1P
145862-22-2P	145862-23-3P	145862-24-4P	145862-25-5P
145862-26-6P	145862-27-7P	145862-28-8P	145862-29-9P
145862-30-2P	145862-31-3P	145862-32-4P	145862-33-5P
145862-34-6P	145862-35-7P	145862-36-8P	145862-37-9P
145862-38-0P	145862-39-1P	145862-40-4P	145862-41-5P
145862-42-6P	145862-43-7P	145862-44-8P	

ROLE: AGR (Agricultural use); BAC (Biological activity or effector, except adverse); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of, as herbicide)

INDEX TERM: 6330-25-2P 70928-90-4P 145862-50-6P 145862-51-7P
145862-52-8P 145862-53-9P 145862-54-0P 145862-55-1P

145862-56-2P 145862-57-3P 145862-58-4P 145862-59-5P
145862-60-8P 145862-61-9P 145862-62-0P 145862-63-1P
145862-64-2P 145862-65-3P 145862-66-4P 145862-67-5P
145862-68-6P 145862-69-7P 145862-70-0P 145862-71-1P
145862-72-2P 145862-73-3P 145862-74-4P 145862-75-5P
ROLE: SPN (Synthetic preparation); PREP (Preparation)
(prepn. of, as herbicide intermediate)

INDEX TERM: 75-44-5, Phosgene 104-12-1, 4-Chlorophenylisocyanate
105-56-6, Ethyl cyanoacetate 105-60-2,
.epsilon.-Caprolactam, reactions 106-47-8,
p-Chloroaniline, reactions 624-83-9, Methyl isocyanate
2216-92-4, Phenylglycine ethyl ester 2521-89-3
84478-65-9 91167-85-0 108310-38-9 145862-45-9
145862-46-0 145862-47-1 145862-48-2 145862-49-3
ROLE: RCT (Reactant)
(reaction of, in prepn. of herbicide)

INDEX TERM: 74-89-5, Methylamine, reactions 107-97-1, Sarcosine
675-20-7, .delta.-Valerolactam 5470-11-1, Hydroxylamine
hydrochloride 25808-30-4 32315-10-9, Triphosgene
70591-20-7 145862-76-6
ROLE: RCT (Reactant)
(reaction of, in prepn. of phenylimidazolone herbicide)

INDEX TERM: 75-45-6, Chlorodifluoromethane 106-96-7, Propargyl bromide
107-30-2, Chloromethyl methyl ether 616-45-5,
2-Pyrrolidinone 18668-72-9
ROLE: RCT (Reactant)
(reaction of, in prepn. of phenylimidazolone herbicide)

L1 ANSWER 7 OF 18 CAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 1993:22158 CAPLUS
DOCUMENT NUMBER: 118:22158
TITLE: Synthesis and gametocidal activity of 1-aryl-5-(aminocarbonyl)-1H-pyrazole-4-carboxylic acids
AUTHOR(S): **Lynch, Michael P.**; Ackmann, Stephen A.; Heim, Dale R.; Davis, George E.; Staszak, Michael A.; Beck, James R.; Tschabold, Edward E.; Wright, Fred L.
CORPORATE SOURCE: DowElanco Res. Lab., Greenfield, IN, 46140, USA
SOURCE: ACS Symp. Ser. (1992), 504(Synth. Chem. Agrochem. III), 200-11
CODEN: ACSMC8; ISSN: 0097-6156
DOCUMENT TYPE: Journal; General Review
LANGUAGE: English
CLASSIFICATION: 28-0 (Heterocyclic Compounds (More Than One Hetero Atom))
Section cross-reference(s): 5

ABSTRACT:
A series of 1-aryl-5-(aminocarbonyl)-1H-pyrazole-4-carboxylic acids were serendipitously discovered to be chem. hybridizing agents. Different synthetic routes were developed for the active analogs depending on whether an electron withdrawing group or electron donating group was present on the Ph ring. Development of the "second generation gametocides" produced analogs which were 5-6 times more active than the original lead. A review with 20 refs.

SUPPL. TERM: review gametocide prepn aminocarbonyl pyrazolecarboxylate; hybridization aminocarbonyl yrazolecarboxylate prepn review

INDEX TERM: Genetics
(hybridization agents, (aminocarbonyl)pyrazolecarboxylates)

INDEX TERM: Plant hormones and regulators
ROLE: RCT (Reactant)
(gametocides, (aminocarbonyl)pyrazolecarboxylates)

INDEX TERM: 145147-06-4D, 5-(Aminocarbonyl)-1H-pyrazole-4-carboxylic acid, 1-aryl derivs.

ROLE: RCT (Reactant)
(hybridization agents and gametocides)

L1 ANSWER 8 OF 18 CAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 1991:122156 CAPLUS
DOCUMENT NUMBER: 114:122156
TITLE: 1-Alkyl-5-cyano-1H-pyrazole-4-carboxamides. Synthesis and herbicidal activity
AUTHOR(S): **Lynch, Michael P.**; Beck, James R.; Tao, Eddie V. P.; Aikins, James; Babbitt, George E.; Rizzo, John R.; Waldrep, T. William
CORPORATE SOURCE: Lilly Res. Lab., Eli Lilly and Co., Greenfield, IN, 46140, USA
SOURCE: ACS Symp. Ser. (1991), 443(Synth. Chem. Agrochem. 2), 144-57
CODEN: ACSMC8; ISSN: 0097-6156
DOCUMENT TYPE: Journal
LANGUAGE: English
CLASSIFICATION: 28-8 (Heterocyclic Compounds (More Than One Hetero Atom))
Section cross-reference(s): 5
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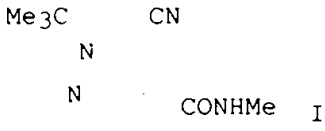

I

ABSTRACT:
A symposium on the investigation of EL-177, 5-cyano-1-(1,1-dimethylethyl)-N-methyl-1H-pyrazole-4-carboxamide, (I) as a new and effective preemergent corn and postemergent cereal herbicide is described. A variety of 1-alkyl-5-cyano-1H-pyrazole-4-carboxamides were prepd. regioselectively using tertiary carbocation chem. With olefins incapable of forming tertiary carbocations, a direct method of alkylating pyrazoles under basic conditions was examd. Regioisomers produced using this method were sepd. by chromatog. Identification of the regioisomers was made by an empirical method comparing the solvent shifts of the pyrazole proton in DMSO-D6 and CDCl3. A comparison of the herbicidal activity of the various pyrazole carboxamides is presented.

SUPPL. TERM: alkylcyanopyrazolecarboxamide prepn herbicide activity symposium; EL177 alkylcyanopyrazolecarboxamide prepn herbicide activity symposium; pyrazolecarboxamide cyanodimethylethylmethyl prepn herbicide activity symposium; structure activity alkylcyanopyrazolecarboxamide herbicide symposium
INDEX TERM: Herbicides
(alkylcyanopyrazolecarboxamides)
INDEX TERM: Molecular structure-biological activity relationship
(herbicidal, of alkylcyanopyrazolecarboxamides)
INDEX TERM: 98477-07-7P
ROLE: BAC (Biological activity or effector, except adverse); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(prepn. and herbicidal activity of)

L1 ANSWER 9 OF 18 CAPLUS COPYRIGHT 2001 ACS

ACCESSION NUMBER: 1990:405585 CAPLUS
DOCUMENT NUMBER: 113:5585
TITLE: Carbon-13 NMR chemical shifts of 1-alkyl-3(5)-cyano-1H-pyrazole-4-carboxylic acid esters
AUTHOR(S): Babbitt, George E.; **Lynch, Michael P.**; Beck, James R.
CORPORATE SOURCE: Lilly Res. Lab., Eli Lilly and Co., Greenfield, IN, 46140, USA
SOURCE: Magn. Reson. Chem. (1990), 28(1), 90-2
CODEN: MRCHEG; ISSN: 0749-1581
DOCUMENT TYPE: Journal
LANGUAGE: English
CLASSIFICATION: 22-10 (Physical Organic Chemistry)
ABSTRACT:
A compilation of 13C NMR chem. shifts for 13 pairs of 3- and 5-cyano-substituted pyrazole regioisomers is reported. All of the ring carbon and cyano carbon 13C chem. shifts show a regular, predictable correlation with the particular isomer, whether 3-cyano or 5-cyano. These shifts occurred in very narrow ranges, precluding any confusion of assignment within the group of compds. studied. X-ray crystallog. anal. was performed on one of the samples.

SUPPL. TERM: NMR alkylcyanopyrazolecarboxylate ester; pyrazolecarboxylate ester alkylcyano NMR carbon
INDEX TERM: Nuclear magnetic resonance
(of alkylcyanopyrazolecarboxylate esters, carbon-13)
INDEX TERM: 33090-55-0 33090-56-1 98477-12-4 119741-58-1
119741-59-2 119741-60-5 121485-81-2 121909-85-1
121909-86-2 121909-87-3 121909-88-4 121909-89-5
121909-90-8 121909-91-9 121909-92-0 127526-68-5
127526-69-6 127526-70-9 127526-71-0 127526-72-1
127526-73-2 127526-74-3 127526-75-4 127526-76-5
127526-77-6 127553-52-0
ROLE: PRP (Properties)
(carbon-13 NMR of)
INDEX TERM: 14762-74-4
ROLE: PRP (Properties)
(nuclear magnetic resonance, of alkylcyanopyrazolecarboxylate esters, carbon-13)

L1 ANSWER 10 OF 18 CAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 1990:114072 CAPLUS
DOCUMENT NUMBER: 112:114072
TITLE: Synthesis and herbicidal activity of 1-aryl-5-halo and 1-aryl-5-(trifluoromethyl)-1H-pyrazole-4-carboxamides
AUTHOR(S): Waldrep, Thomas W.; Beck, James R.; **Lynch, Michael P.**; Wright, Fred L.
CORPORATE SOURCE: Lilly Res. Lab., Greenfield, IN, 46140, USA
SOURCE: J. Agric. Food Chem. (1990), 38(2), 541-4
CODEN: JAFCAU; ISSN: 0021-8561
DOCUMENT TYPE: Journal
LANGUAGE: English
CLASSIFICATION: 5-3 (Agrochemical Bioregulators)
Section cross-reference(s): 28
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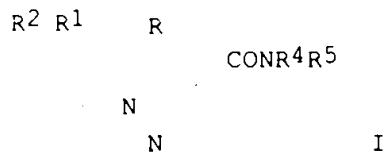


I

ABSTRACT:
A series of 1-aryl-5-halo- and 1-aryl-5-(trifluoromethyl)-1H-pyrazole-4-carboxamides (I, R = Cl, CF3; R1 = R2 = R3 = H, Cl, CF3, OMe, Me; R4 = cyclopropyl, H, Et, Bu, etc.; R5 = Et, Me, OMe) exhibit moderate to strong herbicidal activity in preemergence and postemergence tests. At 1/2 lb/acre, corn, rice, wheat, cotton, and soybean show tolerance, while large crabgrass, foxtail millet, common lambsquarters, redroot pigweed, wild mustard, velvetleaf, jimsonweed, and zinnia were killed or severely injured. A total of 83 5-halo analogs and 47 5-trifluoromethyl analogs were synthesized and their herbicidal activities detd. to examine the structure-activity relationships. The order of activity at C-5 of the pyrazole ring was CF3 > Cl .simeq. Br > I. The order of activity involving substitution on the carboxamide moiety was cyclopropyl .simeq. Me > di-Me > Et > iso-Pr. Substitution on the benzene ring did not result in any major increase in activity when compared with the corresponding Ph analog.

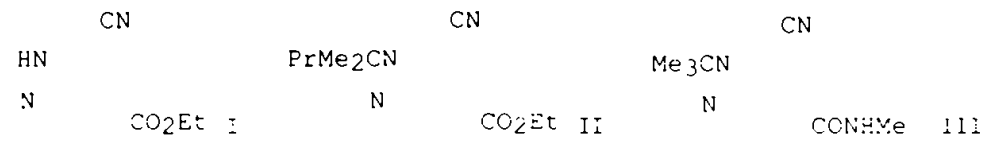
SUPPL. TERM: herbicide halopyrazolecarboxamide deriv
INDEX TERM: Herbicides
(arylhalo and arylfluoromethylpyrazolecarboxamides)
INDEX TERM: Molecular structure-biological activity relationship
(herbicidal, of arylhalo and arylfluoromethylpyrazolecarboxamides)
INDEX TERM: 125024-12-6
ROLE: BIOL (Biological study)
(fluoromethylpyrazolecarboxamide herbicides prepn. from)
INDEX TERM:

98477-04-4P	98533-16-5P	98533-18-7P	98533-21-2P
98533-29-0P	98533-31-4P	98533-32-5P	98533-33-6P
98533-36-9P	98533-44-9P	98533-48-3P	98533-49-4P
98533-53-0P	98533-55-2P	98533-56-3P	98533-57-4P
98533-59-6P	98533-60-9P	98533-65-4P	98533-71-2P
98533-75-6P	98533-79-0P	98533-83-6P	98533-85-8P
98533-87-0P	98533-89-2P	98533-90-5P	98533-93-8P
98533-95-0P	98533-97-2P	98533-98-3P	98533-99-4P
98534-00-0P	98534-01-1P	98534-02-2P	98534-04-4P
98534-06-6P	98534-22-6P	98534-23-7P	98534-24-8P
98534-25-9P	98534-26-0P	98534-27-1P	98534-28-2P
98534-29-3P	98534-30-6P	98534-31-7P	98534-32-8P
98534-33-9P	98534-34-0P	98534-35-1P	98534-36-2P
98534-37-3P	98534-38-4P	98534-39-5P	98534-40-8P
98534-41-9P	98534-43-1P	98534-44-2P	98534-45-3P
98534-47-5P	98534-48-6P	98534-49-7P	98534-50-0P
98534-52-2P	98534-53-3P	98534-54-4P	98534-55-5P
98534-56-6P	98534-57-7P	98534-58-8P	98534-59-9P
98534-60-2P	98534-61-3P	102996-38-3P	125024-11-5P

125048-87-5P
ROLE: AGR (Agricultural use); BAC (Biological activity or effector, except adverse); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. and herbicidal activity of, structure in relation to)

L1 ANSWER 11 OF 18 CAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 1989:477904 CAPLUS
DOCUMENT NUMBER: 111:77904
TITLE: Alkylation studies with 5-cyano-1H-pyrazole-4-carboxylic acid, ethyl ester
AUTHOR(S): Beck, James R.; Aikins, James; **Lynch, Michael P.**; Rizzo, John R.; Tao, Eddie V. P.
CORPORATE SOURCE: Lilly Res. Lab., Div. Eli Lilly and Co., Greenfield, IN, 46140, USA
SOURCE: J. Heterocycl. Chem. (1989), 26(1), 3-6
CODEN: JHTCAD; ISSN: 0022-152X
DOCUMENT TYPE: Journal

LANGUAGE: English
CLASSIFICATION: 28-8 (Heterocyclic Compounds (More Than One Hetero Atom))
Section cross-reference(s): 5
OTHER SOURCE(S): CASREACT 111:77904
GRAPHIC IMAGE:



ABSTRACT:
The title compd. (I) was alkylated regioselectively at N(1) by tertiary carbocations utilizing H2SO4 catalysis and relatively mild conditions. Thus, I was treated with Me2C:CHMe and H2SO4 to give 64% cyano(dimethylpropyl)pyrazolecarboxylate II. In the presence of BF3, the alkylation occurred regioselectively at N(2). Reaction of I with alkyl halides under basic conditions resulted in mixts. of the two isomers with alkylation at N(2) predominating.

SUPPL. TERM: regioselective alkylation cyanopyrazolecarboxylate; alkylcyanopyrazolecarboxamide prepn herbicide; alkylcyanopyrazolecarboxylate

INDEX TERM: Herbicides
(cyanomethylpyrazolecarboxamides)

INDEX TERM: Regiochemistry
(of alkylation of cyanopyrazolecarboxylate with alkenes and alkyl halides)

INDEX TERM: Alkenes, reactions
ROLE: RCT (Reactant)
(regioselective alkylation by, by cyanopyrazolecarboxylate)

INDEX TERM: Alkylation
(regioselective, of cyanopyrazolecarboxylate with alkenes and alkyl halides)

INDEX TERM: 33090-55-0P 33090-56-1P 121909-88-4P 121909-89-5P 121909-90-8P 121909-91-9P 121909-92-0P
ROLE: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation)
(prepn. and amidation of, with methylamine)

INDEX TERM: 119741-58-1P
ROLE: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation)
(prepn. and amidation of, with methylamines)

INDEX TERM: 119741-56-9P
ROLE: BAC (Biological activity or effector, except adverse); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(prepn. and herbicidal activity of)

INDEX TERM: 119741-59-2P 119741-60-5P 121909-85-1P 121909-86-2P 121909-87-3P
ROLE: SPN (Synthetic preparation); PREP (Preparation)
(prepn. of)

INDEX TERM: 108-85-0, Cyclohexyl bromide 137-43-9, Cyclopentyl bromide 513-35-9, 2-Methyl-2-butene 693-89-0 760-21-4 763-29-1, 2-Methyl-1-pentene 816-79-5, 3-Ethyl-2-pentene
ROLE: RCT (Reactant)
(regioselective alkylation by, of

cyanopyrazolcarboxylate)

INDEX TERM: 119741-57-0
ROLE: RCT (Reactant)
(regioselective alkylation of, with alkenes and alkyl halides)

L1 ANSWER 12 OF 18 CAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 1989:212704 CAPLUS
DOCUMENT NUMBER: 110:212704
TITLE: Synthesis of ethyl 2-[(1-aryl-1H-1,2,4-triazol-3-yl)oxy]propionates and related derivatives
AUTHOR(S): Beck, James R.; Babbitt, George E.; **Lynch, Michael P.**
CORPORATE SOURCE: Lilly Res. Lab., Eli Lilly and Co., Greenfield, IN, 46140, USA
SOURCE: J. Heterocycl. Chem. (1988), 25(5), 1467-70
CODEN: JHTCAD; ISSN: 0022-152X
DOCUMENT TYPE: Journal
LANGUAGE: English
CLASSIFICATION: 28-10 (Heterocyclic Compounds (More Than One Hetero Atom))
OTHER SOURCE(S): CASREACT 110:212704
GRAPHIC IMAGE:

RN N

N OH I

ABSTRACT:
Alkylation of 1-aryl-1H-1,2,4-triazol-3-ols I (R = Ph, 2-, 3-, 4-ClC6H5, 3-CF3C6H4, 2,4-Cl2C6H4, 3,4-Cl2C6H4) with MeCHBrCO2Et under basic conditions resulted in the formation of 2-[(1-aryl-1H-1,2,4-triazol-3-yl)oxy]propionic acid, Et esters. No N-alkylated products were detected. Similar alkylation of 2-oxo-5-phenyl-1,3,4-thiadiazole and the corresponding 1,3,4-oxadiazole gave only N-alkylated derivs. With 4-hydroxy-6-phenylpyrimidine and 2-oxo-4-phenylthiazole, both O- and N-alkylation occurred. Structure assignments were based on IR and 13C-NMR spectral data.

SUPPL. TERM: aryltriazolyloxypropionate; aryltriazolol alkylation bromopropionate; triazolol aryl alkylation bromopropionate; thiadiazole oxophenyl alkylation bromopropionate; oxadiazole oxophenyl alkylation bromopropionate; pyrimidine hydroxyphenyl alkylation bromopropionate; thiazole oxophenyl alkylation bromopropionate

INDEX TERM: Regiochemistry
(of alkylation of triazolols, oxothiazoles, oxooxadiazoles, oxothiadiazoles, and hydroxypyrimidine by bromopropionate)

INDEX TERM: Ring closure and formation
(of arylsemicarbazide with orthoformate, aryltriazolol from)

INDEX TERM: Alkylation
(of triazoles, oxothiazoles, oxooxadiazoles, oxothiadiazoles, and hydroxypyrimidines by bromopropionate)

INDEX TERM: Heterocyclic compounds
ROLE: SPN (Synthetic preparation); PREP (Preparation)

(nitrogen, aryltriazolols, prepn. of, via cyclization of arylsemicarbazide with orthoformate)

INDEX TERM: 1199-02-6 3884-31-9 4891-69-4 24028-40-8
ROLE: RCT (Reactant)
(alkylation of, with bromopropionate)

INDEX TERM: 103-03-7 14577-00-5 14580-27-9 14580-28-0 14657-26-2 42158-58-7 57802-85-4
ROLE: RCT (Reactant)
(cyclization of, with orthoformate, aryltriazolol from)

INDEX TERM: 7727-37-9P
ROLE: SPN (Synthetic preparation); PREP (Preparation)
(heterocyclic compounds, nitrogen, aryltriazolols, prepn. of, via cyclization of arylsemicarbazide with orthoformate)

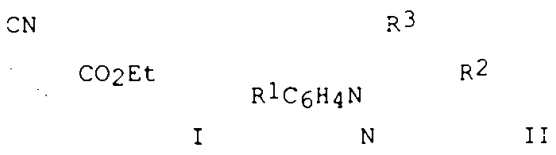
INDEX TERM: 4231-68-9P 37176-51-5P 42158-59-8P 84456-06-4P 84456-12-2P 110626-11-4P
ROLE: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation)
(prepn. and alkylation of, with bromopropionate)

INDEX TERM: 23875-84-5P
ROLE: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation)
(prepn. and alkylation of, with bromopropionate or bromoacetate)

INDEX TERM: 120590-04-7P
ROLE: SPN (Synthetic preparation); PREP (Preparation)
(prepn. of)

INDEX TERM: 110607-55-1P 110607-56-2P 110607-57-3P 110607-58-4P 110607-59-5P 110607-60-8P 110607-65-3P 120590-05-8P 120590-06-9P 120590-07-0P 120590-08-1P 120590-09-2P 120590-10-5P
ROLE: AGR (Agricultural use); BAC (Biological activity or effector, except adverse); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of, as plant growth regulator)

L1 ANSWER 13 OF 18 CAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 1989:8100 CAPLUS
DOCUMENT NUMBER: 110:8100
TITLE: Synthesis of 1-aryl-1H-pyrazolecarbonitriles and related derivatives
AUTHOR(S): Beck, James R.; **Lynch, Michael P.**; Wright, Fred L.
CORPORATE SOURCE: Lilly Res. Lab., Eli Lilly and Co., Greenfield, IN, 46140, USA
SOURCE: J. Heterocycl. Chem. (1988), 25(2), 555-8
CODEN: JHTCAD; ISSN: 0022-152X
DOCUMENT TYPE: Journal
LANGUAGE: English
CLASSIFICATION: 28-8 (Heterocyclic Compounds (More Than One Hetero Atom))
OTHER SOURCE(S): CASREACT 110:8100
GRAPHIC IMAGE:



ABSTRACT:
Chloropyrazoles were treated with NaCN to give nitriles I (R1 = H, Cl). I were converted to pyrazoles II (R2 = CO2H, CONH2, cyano, H, NH2, CO2Me; R3 = CONH2, CO2H, CO2Me, CONHMe).

SUPPL. TERM: pyrazolecarbonitrile carboxy; cyanopyrazolecarboxylic acid
INDEX TERM: 7664-41-7, Ammonia, reactions
ROLE: RCT (Reactant)
(amidation by, of pyrazolecarboxylic acid deriv.)
INDEX TERM: 74-89-5, Methylamine, reactions
ROLE: RCT (Reactant)
(amidation by, of pyrzolecarbonyl chloride deriv.)
INDEX TERM: 117766-97-9P
ROLE: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation)
(prepn. and Curtius reaction of)
INDEX TERM: 117778-62-8P
ROLE: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation)
(prepn. and amidation of)
INDEX TERM: 103053-10-7P
ROLE: SPN (Synthetic preparation); PREP (Preparation)
(prepn. and conversion of, to dicacarboxamide)
INDEX TERM: 117767-01-8P
ROLE: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation)
(prepn. and esterification of, by methanol)
INDEX TERM: 98476-09-6P 98476-16-5P
ROLE: SPN (Synthetic preparation); PREP (Preparation)
(prepn. and hydration of)
INDEX TERM: 117766-90-2P 117766-99-1P
ROLE: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation)
(prepn. and hydrolysis of)
INDEX TERM: 117766-91-3P
ROLE: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation)
(prepn. and reaction of, with thionyl chloride)
INDEX TERM: 98477-01-1P 103053-08-3P 117766-92-4P
ROLE: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation)
(prepn. and reactions of)
INDEX TERM: 117767-02-9P
ROLE: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation)
(prepn. and selective sapon. of)
INDEX TERM: 103053-21-0P 117766-93-5P 117766-94-6P 117766-95-7P
117766-96-8P 117767-00-7P 117767-03-0P 117767-04-1P
ROLE: SPN (Synthetic preparation); PREP (Preparation)
(prepn. of)
INDEX TERM: 117766-98-0
ROLE: RCT (Reactant)
(prepn. reaction of, with sodium azide)
INDEX TERM: 143-33-9, Sodium cyanide
ROLE: RCT (Reactant)
(substitution reaction of, with chloropyrazolecarboxylate esters)
INDEX TERM: 98534-74-8 98534-76-0
ROLE: RCT (Reactant)
(substitution reaction of, with sodium cyanide)

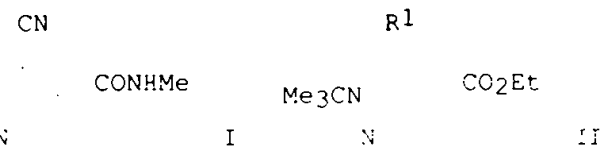
L1 ANSWER 14 OF 18 CAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 1988:75280 CAPLUS
DOCUMENT NUMBER: 108:75280

TITLE: Synthesis of 1-(1,1-dimethylethyl)-1H-pyrazole-4-carboxylate ester derivatives

AUTHOR(S): Beck, James R.; **Lynch, Michael P.**
CORPORATE SOURCE: Lilly Res. Lab., Div. Eli Lilly and Co., Greenfield, IN, 46140, USA

SOURCE: J. Heterocycl. Chem. (1987), 24(3), 693-5
CODEN: JHTCAD; ISSN: 0022-152X
DOCUMENT TYPE: Journal
LANGUAGE: English
CLASSIFICATION: 28-8 (Heterocyclic Compounds (More Than One Hetero Atom))
Section cross-reference(s): 75
OTHER SOURCE(S): CASREACT 108:75280

GRAPHIC IMAGE:



I II

ABSTRACT:
Pyrazolecarboxamide deriv. I was prepd. from pyrazolecarboxylate ester deriv. II (R1 = Me) via II (R1 = CH2Br) and II (R1 = CHO). The cyclocondensation reaction of Me3CNHNH2 with MeCOC(:CHNMe2)CO2Et gave II (R1 = Me).

SUPPL. TERM: cyanopyrazolecarboxamide prepn crystal structure; pyrazolecarboxamide cyano; pyrazolecarboxylate ester

INDEX TERM: Crystal structure
Molecular structure
(of cyanopyrazolecarboxamide deriv.)

INDEX TERM: 74-89-5, reactions
ROLE: RCT (Reactant)
(amidation by, of pyrazolecarboxylate ester deriv.)

INDEX TERM: 141-97-9
ROLE: RCT (Reactant)
(condensation reaction of, with DMF acetal)

INDEX TERM: 4637-24-5, DMF dimethyl acetal
ROLE: RCT (Reactant)
(condensation reaction of, with acetoacetate ester)

INDEX TERM: 94-05-3, Ethyl cyano(ethoxymethylene)acetate
ROLE: RCT (Reactant)
(cycloaddn.-cyclocondensation reaction of, with alkylhydrazine)

INDEX TERM: 7400-27-3
ROLE: RCT (Reactant)
(cyclocondensation reaction of, with (aminomethylene)acetoacetate ester deriv.)

INDEX TERM: 98477-12-4P
ROLE: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation)
(prepn. and amidation of, by methylamine)

INDEX TERM: 98477-08-8P
ROLE: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation)
(prepn. and bromination of)

INDEX TERM: 98477-09-9P
ROLE: SPN (Synthetic preparation); PREP (Preparation)
(prepn. and conversion of, to formylpyrazolecarboxylate analog)

INDEX TERM: 51145-57-4P
ROLE: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation)
(prepn. and cyclocondensation reaction of, with alkylhydrazine)
INDEX TERM: 112779-11-0P 112779-12-1P
ROLE: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation)
(prepn. and dehydration of)
INDEX TERM: 98477-10-2P
ROLE: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation)
(prepn. and oximation of)
INDEX TERM: 112779-14-3P
ROLE: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation)
(prepn. and reaction with nitrosyl chloride and hydrogen chloride)
INDEX TERM: 98477-07-7P 112779-13-2P
ROLE: SPN (Synthetic preparation); PREP (Preparation)
(prepn. of)

L1 ANSWER 15 OF 18 CAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 1987:575941 CAPLUS
DOCUMENT NUMBER: 107:175941
TITLE: Nonaqueous diazotization of 5-amino-1-aryl-1H-pyrazole-4-carboxylate esters
AUTHOR(S): Beck, James R.; Gajewski, Robert P.; **Lynch, Michael P.**; Wright, Fred L.
CORPORATE SOURCE: Lilly Res. Lab., Eli Lilly and Co., Greenfield, IN, 46140, USA
SOURCE: J. Heterocycl. Chem. (1987), 24(1), 267-70
CODEN: JHTCAD; ISSN: 0022-152X
DOCUMENT TYPE: Journal
LANGUAGE: English
CLASSIFICATION: 28-9 (Heterocyclic Compounds (More Than One Hetero Atom))
OTHER SOURCE(S): CASREACT 107:175941
ABSTRACT:
5-Amino-1-aryl-1H-pyrazole-4-carboxylate esters are converted to the corresponding desamino, chloro, bromo, iodo, and methylthio analogs by processes involving nonaq. diazotization. Diazotizing agents are alkyl nitrites except in the case of chlorine where nitrosyl chloride is used.

SUPPL. TERM: diazotization aminopyrazolecarboxylate ester; pyrazolecarboxylate ester; halopyrazolecarboxylate ester
INDEX TERM: Diazotization
(of aminopyrazolecarboxylate esters, in prepn. of deamino and halo analogs)
INDEX TERM: 3107-33-3 19690-59-6
ROLE: RCT (Reactant)
(cycloaddn.-cyclocondensation of, with cyano(ethoxymethylene)acetate ester)
INDEX TERM: 94-05-3, Ethyl cyano(ethoxymethylene)acetate
ROLE: RCT (Reactant)
(cycloaddn.-cyclocondensation of, with phenylhydrazines)
INDEX TERM: 15001-09-9
ROLE: RCT (Reactant)
(diazotization and reaction of, with bromine, pyrazoloindazole deriv. from)
INDEX TERM: 15001-12-4
ROLE: RCT (Reactant)
(diazotization of, in prepn. of bromo analog)
INDEX TERM: 15001-13-5 16459-35-1

ROLE: RCT (Reactant)
(diazotization of, in prepn. of deamino and chloro analogs)

INDEX TERM: 14678-87-6 15001-08-8 16078-71-0
ROLE: RCT (Reactant)
(diazotization of, in prepn. of deamino and halo analogs)

INDEX TERM: 110821-47-1P
ROLE: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation)
(prepn. and cyclization of)

INDEX TERM: 110821-30-2P
ROLE: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation)
(prepn. and diazotization of, in prepn. of brominated deamino compd.)

INDEX TERM: 110821-29-9P
ROLE: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation)
(prepn. and diazotization of, in prepn. of deamino and halo analogs)

INDEX TERM: 885-94-9P 91397-55-6P 98534-71-5P 98534-72-6P
98534-74-8P 98534-76-0P 103053-42-5P 110821-31-3P
110821-32-4P 110821-33-5P 110821-34-6P 110821-35-7P
110821-36-8P 110821-37-9P 110821-38-0P 110821-39-1P
110821-40-4P 110821-41-5P 110821-42-6P 110821-43-7P
110821-44-8P 110821-45-9P 110821-46-0P 110821-48-2P
ROLE: SPN (Synthetic preparation); PREP (Preparation)
(prepn. of)

INDEX TERM: 624-92-0, Dimethyl disulfide
ROLE: RCT (Reactant)
(reaction of, with pyrazolediazonium compd.)

L1 ANSWER 16 OF 18 CAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 1986:442791 CAPLUS
DOCUMENT NUMBER: 105:42791
TITLE: Herbicidal 5-halo-1-halophenyl-1H-pyrazole-4-carbonitriles
INVENTOR(S): Beck, James R.; **Lynch, Michael P.**
PATENT ASSIGNEE(S): Lilly, Eli, and Co. , USA
SOURCE: U.S., 10 pp. Cont.-in-part of U.S. Ser. No. 549,138, abandoned.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
INT. PATENT CLASSIF.:
MAIN: A01N043-56
SECONDARY: C07D231-14; C07D231-16
US PATENT CLASSIF.: 071092000
CLASSIFICATION: 28-8 (Heterocyclic Compounds (More Than One Hetero Atom))
Section cross-reference(s): 5
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 4563210	A	19860107	US 1984-650135	19840913

PRIORITY APPLN. INFO.: US 1983-549138 19831107
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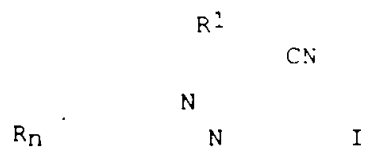

ABSTRACT:
Pyrazolecarbonitriles I (n = 1, 2; R = F, Cl; R1 = halo, CF3), which were prepd., exhibited herbicidal activity. A mixt. of EtOCH:C(CN)2, 2,3,4-Cl3C6H2NHNH2 (prepd. from the resp. aniline), HOAc, and water was refluxed to yield I (Rn = 2,3,4-Cl3, R1 = NH2), and the latter was treated with NOCl in CHCl3 to give I (Rn = 2,3,4-Cl3, R1 = Cl).

SUPPL. TERM: halopyrazolecarbonitrile prepn herbicide; pyrazolecarbonitrile halo prepn herbicide

INDEX TERM: Herbicides
(halo(halophenyl)pyrazolecarbonitriles)

INDEX TERM: 7664-41-7, reactions
ROLE: RCT (Reactant)
(amidation by, of pyrazolecarboxylic acid deriv.)

INDEX TERM: 5446-18-4
ROLE: RCT (Reactant)
(cycloaddn.-cyclocondensation of, with (ethoxymethylene)acetoacetate ester deriv.)

INDEX TERM: 123-06-8 571-55-1
ROLE: RCT (Reactant)
(cycloaddn.-cyclocondensation of, with phenylhydrazine deriv.)

INDEX TERM: 58791-79-0
ROLE: RCT (Reactant)
(deamination-bromination of)

INDEX TERM: 79002-96-3 102996-25-8
ROLE: RCT (Reactant)
(deamination-chlorination of)

INDEX TERM: 98534-78-2P
ROLE: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation)
(prepn. and amidation of)

INDEX TERM: 80025-74-7P
ROLE: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation)
(prepn. and cycloaddn.-cyclocondensation of, with (ethoxymethylene)malononitrile)

INDEX TERM: 80025-46-3P
ROLE: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation)
(prepn. and deamination-chlorination of)

INDEX TERM: 102996-38-3P
ROLE: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation)
(prepn. and dehydration of)

INDEX TERM: 98534-77-1P
ROLE: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation)
(prepn. and sapon. of)

INDEX TERM: 102996-23-6P 102996-24-7P 102996-26-9P 102996-27-0P
102996-28-1P 102996-29-2P 102996-30-5P 102996-31-6P
102996-32-7P 102996-33-8P 102996-34-9P 102996-35-0P
102996-36-1P 102996-37-2P 102996-39-4P 102996-40-7P
ROLE: AGR (Agricultural use); BAC (Biological activity or effector, except adverse); SPN (Synthetic preparation); BIOL

(Biological study); PREP (Preparation); USES (Uses)
(prepn. of, as herbicide)

INDEX TERM: 634-67-3
ROLE: RCT (Reactant)
(N-nitrosation of, and redn. of product from)

L1 ANSWER 17 OF 18 CAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 1986:222875 CAPLUS
DOCUMENT NUMBER: 104:222875
TITLE: Pyrophosphohydrolase activity and inorganic pyrophosphate content of cultured human skin fibroblasts. Elevated levels in some patients with calcium pyrophosphate dihydrate deposition disease
AUTHOR(S): Ryan, Lawrence M.; Wortmann, Robert L.; Karas, Barbara; **Lynch, Michael P.**; McCarty, Daniel J.
CORPORATE SOURCE: Dep. Med., Med. Coll. Wisconsin, Milwaukee, WI, 53226, USA
SOURCE: J. Clin. Invest. (1986), 77(5), 1689-93
CODEN: JCINAO; ISSN: 0021-9738
DOCUMENT TYPE: Journal
LANGUAGE: English
CLASSIFICATION: 14-11 (Mammalian Pathological Biochemistry)
ABSTRACT:
In Ca pyrophosphate dihydrate (CPPD) crystal deposition disease, metabolic abnormalities favoring extracellular inorg. pyrophosphate (PPi) accumulation have been suspected. Elevations of intracellular PPi in cultured skin fibroblasts from a single French kindred with familial CPPD deposition and elevated nucleoside triphosphate pyrophosphohydrolase activity (NTPPPH), which generates PPI in exts. of CPPD crystal-contg. cartilages favor this suspicion. To det. whether NTPPPH activity or PPi content of cells might be a disease marker expressed in extraarticular cells, human skin-derived fibroblasts were obtained from control donors and patients affected with the sporadic and familial varieties of CPPD (CPPD-S and CPPD-F) deposition. Intracellular PPi was elevated in both CPPD-S and CPPD-F fibroblasts compared with control fibroblasts. Ecto-NTPPPH activity was elevated in CPPD-S but not in CPPD-F. Intracellular PPi correlated with ecto-NTPPPH. Elevated PPi levels in skin fibroblasts may serve as a biochem. marker for patients with familial or sporadic CPPD crystal deposition disease; ecto-NTPPPH activity further separates the sporadic and familial disease types. Expression of these biochem. abnormalities in nonarticular cells implies a generalized metabolic abnormality.

SUPPL. TERM: calcium pyrophosphate dihydrate deposition fibroblast biochem; pyrophosphohydrolase calcium pyrophosphate dehydrate deposition
INDEX TERM: Fibroblast
(pyrophosphates and pyrophosphohydrolase of human, in calcium pyrophosphate dihydrate crystal deposition disease)
INDEX TERM: 17031-92-4
ROLE: BIOL (Biological study)
(crystals, deposition of, pyrophosphates and pyrophosphohydrolase of human fibroblasts in)
INDEX TERM: 9027-73-0 9033-44-7 9075-54-1
ROLE: BIOL (Biological study)
(of fibroblast, in calcium pyrophosphate dihydrate crystal deposition disease in humans)

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